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Multiple Myeloma—Some Clinical and Protein Variants

By

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THE introduction of electrophoresis by Tiselius in 1937[1] stimulated much interest in multiple myeloma. This was so, not only because electrophoresis was a useful tool in the diagnosis of multiple myeloma, but also because the application of this technique to the study of myeloma globulins promised to increase understanding of protein chemistry.

The introduction of paper electrophoresis[2,3] has made the procedure available to every clinical laboratory. It has generally replaced the time-honored salting-out technique because of its greater accuracy in distinguishing between the albumin and globulin fractions.

Data obtained by electrophoresis can be most helpful in the diagnosis of some cases of multiple myeloma if cognizance is taken of the great variability of patterns.

A few remarks regarding the basic problems of paper electrophoresis should be made. The serum or other protein solution to be tested is placed on a strip of filter paper saturated with a buffer solution, usually pH 8.6. The strip is stretched between electrodes. Electrodiffusion is allowed to proceed for several hours, after which time the strip is fixed and stained. As pH 8.6 most of the serum proteins are negatively charged and migrate towards the anode. The rate of movement is proportional to the negative charge. The stained strip shows spots representing the postion of each protein group at the termination of the test. A graph is then derived from the strip by means of the photodensitometer. Fig. 1 shows the strip obtained by the electrophoresis of normal serum and the graph derived from it.

The graph reveals three things:

1. The degree of negative charge: Albumin is the most negative serum protein and therefore migrates most rapidly. Following this are the successively slower proteins bearing the designations α, β and γ. These complexes may be split into α_1, and α_2, as well as fast and slow γ fractions. Occasionally complexes are seen in intermediate positions.

2. The quantity of each protein is proportional to the intensity of staining: The photodensitometer graphs and records these spots quantitatively.

3. The degree of homogeneity or heterogeneity of a protein complex: A high narrow peak suggests a homogenous protein as seen characteristically in multiple myeloma.

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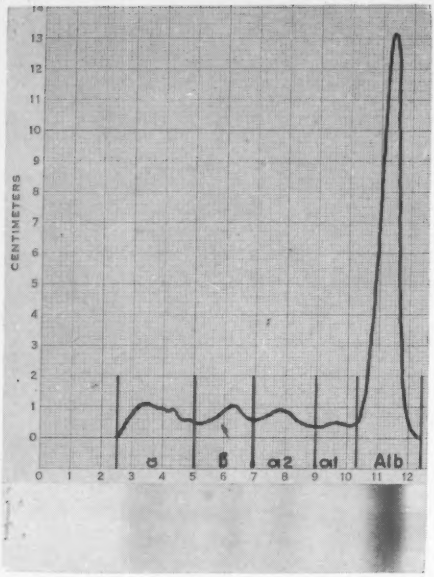

FIG. 1. Stained filter paper strip obtained by electrophoresis of pooled normal serum and graph derived from it.

A broad based rise suggests a heterogeneous protein group, e.g., a mixture of proteins which have slightly differing charges.

It should be noted that electrophoresis is not a conclusive method of protein identification. A single spot may contain proteins of different molecular weights and exhibit different immunologic and chemical properties.

Multiple myeloma, usually a disease of middle and late life, is characterized by the invasion of the red marrow by abnormal plasma cells, often producing osteolytic lesions, pain and pathologic fractures. This invasion of the marrow may result in anemia or hemorrhagic disturbances. Abnormal proteins are often found in the serum and urine. The disease is slowly progressive and invariably fatal.

Laboratory help is most useful in those diseases which exhibit variable manifestations. Multiple myeloma is characterized by a moderate degree of pleomorphism. In general, however, a thread of uniformity runs through this disease so that it is one of the easiest to recognize, especially by x-ray. It also frequently produces an electrophoretic pattern which is virtually diagnostic. Unfortunately, not all cases are so obliging. As additional data concerning multiple myeloma and electrophoresis accumulate, periodic reexamination of these subjects is desirable.

Multiple myeloma may vary as to clinical picture, age of onset and rapidity of course. It may also exhibit marked variations in laboratory findings, particularly with respect to serum and urinary proteins. Several of these variants will be illustrated by appropriate cases selected from a series of 19 proved cases of multiple myeloma encountered during the past 10 years at Bay Pines Veterans Administration Hospital. These will include the following: I. Survival time, II. Hemorrhagic forms, and III. Neurologic manifestations.

PART I—CLINICAL VARIANTS

I. Survival time after the onset of initial symptoms.

The authors are cognizant of the difficulty of determining the actual duration of multiple myeloma, since it may exist many years prior to the development of symptoms. In fact, in one of our cases (G.J.) it was discovered by a routine chest film. However, for practical reasons we have calculated the duration of the disease from the time of discovery or the occurrence of severe bone ache or pathologic fractures.

There is a widespread impression that multiple myeloma is a relatively slow process. However, in this series nine patients died within six months after the first symptom.

The description of a particularly fulminating case follows:

Case C.H.—illustrating an exceedingly high globulin level, a rapid course, hemorrhagic manifestations and absence of radiologic bone changes. This 65 year old white male was admitted to the otolaryngological service because of bleeding from the left nostril. Except for mild dyspnea he had no other complaints. His past history, fam-

ily history and systems review were noncontributory.

Physical Examination: The patient was 66 inches tall, weighed 149 pounds. He was afebrile and his blood pressure was 164/100. There was some pallor but the patient appeared alert. The salient findings were blood clots about the nostrils and posterior nasopharynx and oozing of blood from the floor of the left nasal cavity. The chest, heart, lungs, abdomen and genitalia were normal except for a well healed right lower quadrant abdominal scar. The liver and spleen were not palpable. There were swelling and mottled bluish discoloration of the terminal phalanx of the right middle finger.

On admission the chest x-ray showed slight left ventricular enlargement, elevation of the right leaf of the diaphragm and increased hilar and lung markings. The electrocardiogram showed left ventricular hypertrophy and runs of nodal extra beats.

At the time of admission his WBC was 7,000 with 51% neutrophils, 39% lymphocytes, 8% monocytes, 1% eosinophils and 1% basophils. The RBC was 2.21 million, hemoglobin 42%, hematocrit 23% and the platelet count 243,100. Clot retraction was complete in 3 hours; the prothrombin time was 15.9 seconds or 52% of the daily normal control. The BUN was 12.2 mg. % and the blood glucose 93 mg. %; serum bilirubin was 0.4 mg.%; thymol turbidity 0.5 units.

Urinalysis showed the following: 4+ albumin, 2 finely granular casts, 10-15 RBC/HPF. A repeat urinalysis was negative for albumin and sugar. Urine specimens were negative for Bence-Jones protein.

The total serum protein was 14.6 grams %, of which 1.6 grams % was albumin and 13.0 grams % globulin.

X-ray studies of the bones disclosed small osteolytic lesions scattered throughout the spine, pelvis and femora.

The hospital period was uneventful except for repeated small epistaxes. His treatment included 5 units of bolod, digitalis, aminophyllin and serpasil. He was discharged improved.

Five days later the patient reapplied for hospitalization because of recurrent nosebleed and petechiae over his entire body. The petechiae first appeared on the forearms but later became generalized. Physical examination merely showed purplish-red macules over the trunk and extremities and clots about the nares.

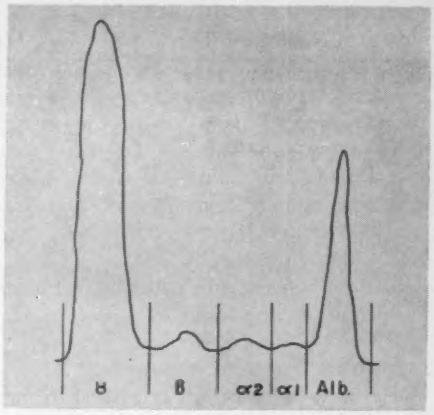

FIG. 2. Electrophoretic pattern of C.H.

Urinalyses showed 4+ albumin and now were consistently positive for Bence-Jones protein. The specific gravity was fixed at 1.008 and the sediment contained casts, red and white cells.

At this time the serum proteins were 20.2 grams %, of which 1.4 grams % were albumin and 18.8 grams % globulin. Fig. 2 shows the electrophoretic pattern.

On readmission the BUN was 25 mg. %, but it rapidly rose to 152 mg. prior to death. The hematocrit was 21.5%, hemoglobin 44%, and the RBC 2.14 million. The WBC was 5,200 per cu.mm., with 61% neutrophils, 21% lymphocytes, 5% monocytes, 10% eosinophils and 3% bands. One week following admission his WBC fell to 2,900, with 17% neutrophils, 54% lymphocytes, 16% monocytes, 7% eosinophils, 6% basophils and plasma cells. The terminal WBC was 11,000 per cu.mm., with 49% neutrophils, 35% lymphocytes, 12% monocytes, 2% eosinophils and 2% basophils.

Although the petechiae subsided, epistaxis persisted. Nine days after admission the

temperature rose to 105°F and was associated with oliguria of 50 cc. in 24 hours, the urine being bloody. He sank into uremic coma and expired 53 days following his initial admission.

The autopsy showed:

1. Plasma cell infiltration of the spleen, bone marrow, lymph nodes, vertebrae and kidneys.
2. Chronic pyelonephritis.
3. Bronchopneumonia with purulent bronchitis.
4. Coronary atherosclerosis.
5. Acute ulcerative esophagitis.

The early stages of this disease, characterized by hemorrhagic manifestations, weight loss and hyperglobulinemia suggest macroglobulinemia. Unfortunately, an ultracentrifuge was not then available to confirm this. The fulminating course (53 days) is also interesting and is suggestive of acute leukemia. The high protein is remarkable,[4] although an even higher level (23.3 grams) was reported by Wintrobe in *Clinical Hematology*.

Table 1 lists the survival time of the other patients in this series, together with some additional data.

The wide range of survival times has its counterpart in other lymphomas, e.g., acute and chronic leukemias. However, in this series there was no tendency for the younger victims to have a more fulminating course. Except for two cases, most of the patients were in their 50's and 60's. X-ray evidence of osseous involvement was present in all but one patient, who exhibited predominantly hemorrhagic manifestations.

In a series of 55 cases of multiple myeloma reported by Snapper in 1953,[5] most of the patients died between six months to one year after the onset of symptoms. The average survival time was 20 months. The age incidence was also similar to that encountered in the present series.

As can be seen from Table I, low serum globulin levels are no guarantee of long survival. Possibly the fulminating hemorrhagic course of C.H. was attributable to the exceedingly high globulin, for some maintain that the increased viscosity predisposes to small hemorrhagic infarctions.

The deposition of abnormal proteinaceous material (para-amyloid) results in the "myeloma kidney" and impaired renal function.

Although over 50% of the patients had azotemia, a definite diagnosis of myeloma kidney was made in only two (C.H. and E.R.). Three additional patients showed changes suggestive but not diagnostic of myeloma kidney. The patient (R.S.) with the highest BUN (176) was not autopsied. Possibly some of the less severe azotemias resulted from less extensive renal amyloid involvement plus the usual sclerotic changes so common in patients of this age group.

Although all of these patients suffered from repeated severe infections, mainly bronchopneumonia, they responded well to antibiotics. The later stages were usually associated with azotemia.

The more severe skeletal deformities were usually seen in the longer survivors. However, the 12-year survivor showed virtually no progress of his early osseous lesions.

No attempt will be made to evaluate the effect of therapy in these cases. Any conclusions as to the value of treatment in any but very large series should be viewed with skepticism, since the more benign cases will live long enough to have more therapy than the rapidly fatal ones.

II. Multiple myeloma with hemorrhagic manifestations and absence of osseous lesions.

The previous case (C.H.) presented a hemorrhagic picture but exhibited typical roentgenologic bone changes. The case to be described more closely resembles the macroglobulinemic syndrome. The sedimentation constant of this globulin is unknown.

Case H.S. This 65-year old white male was first admitted to Bay Pines March 8, 1957 with complaints of epistaxis, hemoptysis and dyspnea for six months.

Physical examination showed the patient to be severely dyspneic and cyanotic. There were blood clots about his nostrils. Examination of the chest disclosed bilateral moist

TABLE 1

SOME IMPORTANT FINDINGS IN 19 CASES OF MULTIPLE MYELOMA

Name	Age	Survival	Bone Lesions X-ray	Total Glob.	Peak	Infections	BUN	Calc.	Rx.**
C.H.	65	53 days	+	18.8	γ*	Pneumonia	152		No
R.S.	61	90 days	+	3.9	Non-Dg.**	Pneumonia	176	11.1	Ur.
L.W.	59	90 days	+	5.35		No	43	11.4	No
B.W.	55	5 mos.	+	4.6		Febrile	Nephrosis	9.6	X-ray
B.R.	37	6 mos.	+	2.4		Pneumonia	42.8	16.0	Ur., Ster.
C.G.	51	1 yr.	+	8.0		No	47	15.0	Stilb.
B.B.	57	1 yr.	+	6.3			60	12.9	X-ray
A.A.	68	14 mos.	+	6.1		Tbc.	72	14.5	Ur., Stilb.
G.J.	64	1+ yr.?	+	4.08	β	No	23	11.2	No
H.S.	65	2 yrs.	0	10.74	γ*	Pneumonia	56		Ster.
J.R.	64	3 yrs.	+	7.02	γ*	Tbc., Pneum.		13.0	Ur., X-ray
W.W.	64	5 yrs.	+	2.15	Non-Dg.	Pneumonia		9.7	Ur., Ster.
T.W.	34	6 yrs.	+	5.35			29.5		Ur.
E.R.	73	12 yrs.	+	3.52	α_2		149	11.3	X-ray
A.L.	65	10 wks.	+	2.95	Non-Dg.	No	8	10.2	Ur.
J.S.***	67	1 yr.	+	4.3		No		15.8	Ur., Ster.
A.M.***	63	1 yr.	+	1.51	Hypo γ	No	59	13.7	Ur., Ster.
L.M.***	38	2 yrs.	+	3.74	γ	No	7	10.8	Ur., X-ray, NM
W.M.***	60	4 yrs.	+	1.63	Hypo γ	Pneumonia	37	15.0	Ur., Myl., NM

* Homogeneous.

** Ur. = Urethane; Ster. = Steroids; Stilb. = Stilbamidine; NM = Nitrogen Mustard; Myl. = Myleran; Non Dg. = Non-diagnostic.

*** Still living.

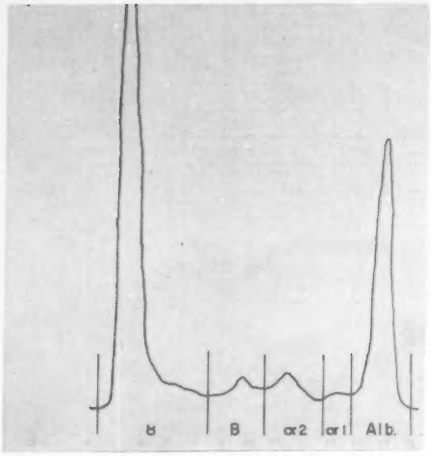

FIG. 3. Electrophoretic pattern for H.S.

râles. The blood pressure was 160/90. The heart was rapid and regular but no murmurs were heard. No abnormalities were noted in the abdomen. The significant laboratory data were hemoglobin below 48%, hematocrit 22, WBC 5,000, with 27% neutrophils, 36% lymphocytes, and 37% monocytes. On the following day the WBC rose to 18,200. The urine was negative except for 1+ albumin. Bence-Jones protein was absent. The platelet count was 187,000.

The serum contained 3 grams % of albumin and 10.74 grams % of globulin. The electrophoretic pattern is shown in Fig. 3.

X-ray showed consolidation of the right upper lobe. Sputum examination showed candida albicans. The pneumonitis gradually cleared with antibiotics. X-rays of the bones were negative. A neurologic consultation was secured March 31, 1958 because of ataxia and swaying even when sitting. The neurologist described spontaneous nystagmus. The biceps, triceps and Hoffman reflexes were more active on the left than the right. Hypotonia was present. There was no past pointing. The neurologist's impression was "myelopathy of the cerebellum and brain stem due to toxins of multiple myeloma."

Hospital course: At first his generalized weakness responded to oxygen and transfusions and the febrile episodes to antibiotics, but no change was observed in the neurologic picture.

However, he had recurrent febrile episodes and progressive weakness. He died Oct. 20, 1958, two years after the onset of his first symptom.

Autopsy revealed the following:

1. Pulmonary emphysema.
2. Bronchopneumonia.
3. Empyema, left.
4. Plasmocytosis of the marrow.
5. Cirrhosis.
6. Osteoporosis.

III. Neuropathy in Multiple Myeloma.

Neuropathy unrelated to skeletal abnormalities or to myelomatous infiltration has been observed frequently in multiple myeloma. The following case presents typical findings of this condition.

Case W.W. This 61 year old white auto supply salesman was admitted to Bay Pines VA Hospital Aug. 8, 1955 with a history of progressive weakness in the calf muscles of both legs since August 1954, loss of power in the legs since September 1954, and weakness and loss of coordination of both forearms and hands. These symptoms were first attributed to combined system disease, but despite Vitamin B_{12}, weakness increased so that he was unable to walk. His arms and hands then became very weak. Numbness and tingling in his hands and feet were troublesome.

Physical Examination: The patient was a well developed and nourished 61 year old, alert white male. He was unable to stand because of loss of strength in both feet and legs. There was also marked weakness of both arms. Eyes: no nystagmus, pupils equal and reacted to light and accommodation. Ears, nose and throat: negative. Tongue: red but not atrophic. Moist râles were present in both lung bases. The heart was not enlarged. Systolic murmurs were heard over the mitral and aortic areas. The abdomen was negative except for an enlarged liver.

Neurologic Examination: There was weakness of all extremities and back. He was unable to stand unassisted. The intrinsic

muscles of both hands, particularly the thenar and hypothenar muscles, had undergone atrophy.

There was marked weakness of the legs and complete loss of power in the feet. Cranial nerves were normal. The upper abdominals were present, the lowers absent. The cremasterics were active bilaterally. All tendon reflexes were absent. The Babinski and Hoffman reflexes were not obtainab'e. Vibratory sense was poor to absent in all extremities. Except for 2 point discrimination there was no other sensory loss.

X-ray and laboratory examinations: Hematology: WBC 6,200; hematocrit 42%. Urinalysis: specific gravity 1.012, albumin and sugar negative, microscopic negative. Blood chemistry: BUN 10.8 mg. %, glucose 114 mg. %, serum calcium 9.7 mg. %, inorganic phosphorus 4.25 mg. %, acid phosphatase 0.53 units (King-Armstrong), alkaline phosphatase 1.55 units (King-Armstrong), cholesterol 178 mg. %. The total protein was 4.8 grams %, albumin 2.65 grams %, globulin 2.15 grams %. See electrophoretic pattern, Fig. 4 (W.W.).

Stools were negative for ova, parasites and blood. Liver "profile": Cholesterol 178 mg. %, serum bilirubin 0.3 mg. %, van den Bergh, direct: no, indirect: yes. Alkaline phosphatase 1.55 units; thymol turbidity 14.5 units.

Five tests for Bence-Jones proteinuria were positive. X-ray studies showed osteolytic lesions in the pelvis and vertebral bodies of L_3 and L_4. The ribs were negative. The G.I. series and urogram were negative. The electrocardiogram was normal. Biopsy of an inguinal lymph node showed no diagnostic changes. A bone biopsy from an osteolytic lesion in the pelvis showed plasma ce'l myeloma.

Diagnosis: Plasma cell myeloma with neuropathy.

Hospital Course: The patient was treated with one gram of urethane 4 times daily. The muscle weakness of his legs gave way to contractures. He developed ascites which required frequent paracentesis. Thereafter he deteriorated rapidly and died March 26, 1959.

Important autopsy findings were:

1. Multiple myeloma.
2. Coronary atherosclerosis.
3. Arteriolonephrosclerosis.
4. Atrophy of adrenals.
5. Generalized atrophy of the muscles of the extremities.

It is important to note that there were no focal lesions of the spinal cord.

Microscopic examination of the spinal cord showed a decrease of cellular content of the anterior horns and marked degeneration of the cells. The posterior tracts contained numerous grayish-white psammoma bodies and under myelin stain showed advanced demyelinization of the posterior and lateral spinal tracts.

Neuropathy resulting from cranial and spinal lesions is to be anticipated in multiple myeloma, as in case E.R., to be described. However, as early as in 1899[6] neurological abnormalities were observed which could not be attributed to osseus defects or to myelomatous invasion of the central nervous system or the peripheral nerves. Subsequent workers[7,8,9] postulated that the neuropathy was due to the toxic effect of myeloma proteins. Several investigators[10,11] reported cases exhibiting neuropathy similar to that seen in our case and attributed the neural dysfunction to a specific neurotoxin.

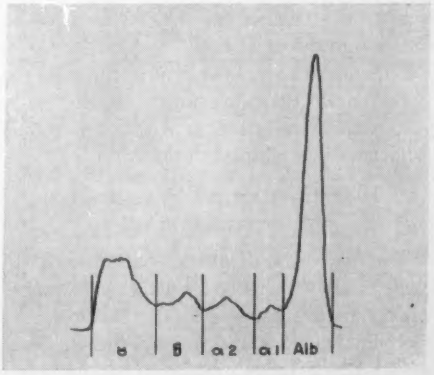

FIG. 4. Electrophoretic pattern for W.W.

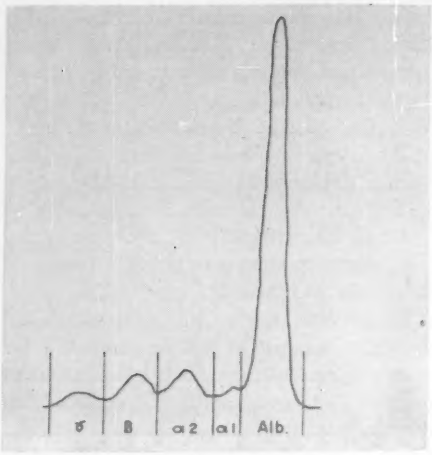

FIG. 5. Electrophoretic pattern of C.M.

It was the belief of the consulting neurologist that the cerebellar signs in case H.S. were also due to a neurotoxic effect of multiple myeloma. However, in that case anemia was very severe and may have contributed to this phenomenon, as suggested by Davison.[12] In case W.W., however, the very severe changes could not be attributed to anemia, myelomatous infiltration or pressure on the cord or roots due to spinal defects. Histologic examination of the cord showed degeneration of the cells and demyelinization of the posterior and lateral tracts.

This type of neuropathy may be a more frequent complication than suspected from the literature, since most neurologic changes would be attributed to skeletal changes so common in this condition.

The almost monotonous uniformity of the symptoms in cases previously reported suggests that there is indeed a true neurotoxic syndrome in multiple myeloma.

PART II—PROTEIN VARIANTS IN MULTIPLE MYELOMA

The discussion of protein variants will include cases which illustrate the wide ranges of serum protein levels, the less common globulin fractions and, finally, the incidence of the Bence-Jones protein.

I. Hypogammaglobulinemia in multiple myeloma. (Figs. 5, 6, 7)

Case C.M. This 56 year old white male presented a 3-month history of 15 pounds weight loss and migratory pains in his abdomen, shoulders and lumbar region.

Significant laboratory findings were as follows: Urine, glucose 4+, albumin negative. Bence-Jones protein positive on two occasions.

X-ray studies disclosed numerous small radiolucent areas in the humeri, femora, skull, ribs and shoulders.

The hematocrit was 35% and WBC 5,000, with a normal differential and no abnormal cells.

The electrophoretic pattern of the serum was: albumin 4.2 grams %; globulin α_1, 0.20, α_2, 0.83, β 0.48, γ 0.12.

While under observation he developed recurrent pulmonary infections which responded to antibiotics. In spite of treatment with urethane, myleran, nitrogen mustard and steroids, his kyphosis has increased. He is still alive but gradually losing ground.

It is evident that the important factor in multiple myeloma is the cell itself. It may produce typical manifestations of multiple myeloma while lacking the ability to elaborate abnormal proteins. In this respect multiple myeloma resembles lymphatic leukemia, in which approximately 50% of the patients have hypoglobulinemia,[13,14,15] presumably resulting from interference with the function of normal plasma cells.

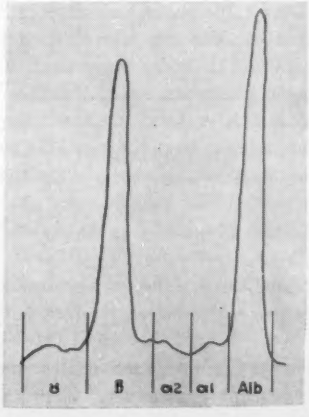

FIG. 6. Electrophoretic pattern of G.J.

Although the most characteristic electrophoretic pattern in multiple myeloma is a high spike in or near the γ position, many cases are characterized by proteins which migrate as α or β globulins.

II. Multiple myeloma with beta globulin.

Case G.J. This 64 year old colored male entered Bay Pines Hospital Oct. 19, 1959 because of edema and dyspnea. He gave a history of hypertension and dyspnea for two years. Although he denied chest pain, he stated that he had severe backache for many years. Edema was of recent origin but he was unable to give an accurate past history and systems review.

Physical examination showed a 64-year old colored male, acutely and chronically ill, with severe anasarca, orthopnea, dyspnea, and venous engorgement. His sensorium was clouded. The pulse was 100, blood pressure 188/110, temperature 97.4. Evidence of free fluid was noted in both pleural cavities.

Fine crepitant râles were heard in both lung bases. The heart was enlarged, rate 100, rhythm regular, diastolic gallop. A grade 1 systolic apical murmur was present.

The liver edge could be felt 4 cm. below the costal margin through the edematous abdominal wall, but ascites was absent. There was 4+ pitting edema of the legs; otherwise the physical examination was not remarkable.

Laboratory data: WBC 2,700; neutrophils 86%, monocytes 4%, eosinophils 2%, lymphocytes 8%. Hemoglobin 57%, hematocrit 26; BUN 23 mg. %. Urinalysis: specific gravity 1.004, albumin 2+, occasional hyaline casts. Blood sugar 93 mg. %. Bence-Jones protein negative. Total protein 6.8 grams %, albumin 1.72 grams %, globulin 4.08 grams %.

V.D.R.L. non-reactive. Alkaline phosphatase 5.3 units (King-Armstrong), acid phosphatase 2.7 units (King-Armstrong), calcium 11.2 mg. %, phosphorus 2.3 mg. %.

Final blood count: WBC 1,150; neutrophils 68%, lymphocytes 28 %, monocytes 3%, eosinophils 1%. RBC 3.62, hemoglobin 74%, platelets 181,000; hematocrit 35.

Bone marrow aspiration showed nothing but plasma cells. On a chest film of 10/20/59 the heart appeared enlarged. Lungs showed increased markings suggestive of pulmonary congestion; osteolytic areas in bones of both shoulders.

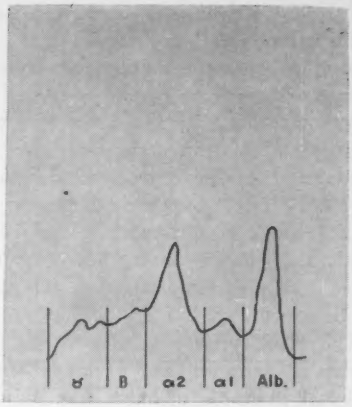

FIG. 7. Electrophoretic pattern of E.R.

Bone survey showed osteolytic areas involving most of the skeleton. There were numerous compression fractures involving the dorsal and lumbar vertebral bodies. Electrocardiogram showed "left" ventricular strain.

Hospital course: Following digitalization and diuretics there was excellent diuresis and subsidence of edema. However, the patient became progressively weaker and expired 12/3/59, 45 days after admission.

Necropsy revealed:

1. Multiple myeloma.
2. Hypertensive heart disease.

III. Multiple myeloma with an alpha$_2$ globulin pattern:

Case E.R. This 73-year old white male first sought medical aid in 1947 because of severe pain in his left hip for two years. Physical examination was not remarkable except for tenderness and painful limitation of motion of the left hip.

The significant laboratory findings in 1947 were 4+ albuminuria, WBC 10,000, and hemoglobin 15 grams. The serum consisted of 3.52 grams % of albumin and 1.18 grams % of globulin.

Serum calcium was 11.3 mg. %, phosphorus 4.1 mg. % and alkaline phosphatase 3.5 units (King-Armstrong). X-ray showed

a large destructive cystic lesion involving the entire left half of the pelvis. A biopsy of the left ilium showed clusters of abnormal plasma cells.

Although his only treatment was x-ray therapy of the hip lesion, the condition seemed stabilized, except for compression of the third cervical vertebral body.

In 1955 he complained of aching in the hands and grinding in the neck. Again the urine was repeatedly negative for Bence-Jones protein.

The blood picture was not remarkable. Serum proteins were 3.7 grams % albumin and 3.52 grams % globulin. The BUN was 149. X-rays showed no new lesions except osteolytic areas in both humeri.

Physical examination was essentially as before, but with the addition of neural involvement of both upper extremities and bilateral Horner's syndrome, presumably resulting from the spinal lesion.

He was followed as an outpatient and died at home 12 years after the onset of his symptoms.

This case is interesting because he was our longest survivor despite the reputation of alpha myeloma for extreme malignancy.

The diversity of protein patterns in multiple myeloma was first noted in 1939 by Longsworth et al.,[16] who reported two cases with increased gamma globulin and a third with a normal pattern. Kekwick[17] found that the major protein component of four of his cases migrated with gamma globulins, while a fifth behaved as a beta. Gutman[18] employed the letter M to describe the myeloma globulin fraction migrating between β and γ. Many workers seem to employ this symbol for any myeloma globulin regardless of its position in the spectrum. Wuhrmann et al., [19] confirmed the existence of β and γ globulin and also encountered α myeloma globulins as well as normal patterns. In a series of 60 cases, 12 were of the α type. In general, the α globulin increases were more modest than in the γ cases. Other α cases were reported by Sandkuhler,[20] Ludin[21] and Griffiths.[22,23] Of 44 cases of multiple myeloma studied by Snapper,[5] γ patterns were found in 4, β in 6, γ in 21, and only minor abnormalities in 13. Conn[24] and associates reported that all of their 18 cases of multiple myeloma had abnormal proteins and that in 14 (78%) the electrophoretic pattern was diagnostic. In about half of Conn's cases, the abnormal protein migrated as a γ complex. In the remainder it migrated between γ and β, as β or as α, in order of diminishing frequency.

Twenty-five per cent of his cases showed non-diagnostic abnormalities. In his review of 50 previously reported cases of multiple myeloma, the electrophoretic patterns were as follows: α 4%, β 16%, between β and γ 12%, γ 54%, abnormal but nonspecific 12%, and normal patterns 2%.

Glenchur et al.,[25] found that in his 51 cases of multiple myeloma the protein spectra were as follows: γ 49%, β 16%, "M" (between γ and β) 10%, slow γ 19%, normal 6%. In this series, those with β globulin had the shortest survival.

TABLE 2

PERCENTAGE INCIDENCE OF ABNORMAL GLOBULINS IN THE PRESENT SERIES OF CASES OF MULTIPLE MYELOMA COMPARED WITH FINDINGS OF THREE OTHER INVESTIGATORS

Collected by	Number of Cases	α_1	α_2	β	"M" β−γ	γ	Abnormal but Non-specific	Normal	Hypoglobulin
Conn	50	4		16	12	54	12	2	
Glenchur	51			16	10	68		6	
Wall	62			10		80			10
Present Series (having electrophoretic patterns)	10		10	10		40	10	10	20

In Wall's[26] series of 62 cases of multiple myeloma, the myeloma protein migrated as β in 10%, γ in 80% and no myeloma protein in 10%. Those lacking myeloma protein showed hypogammaglobulinemia.

The latter cases are similar to patients in our series with hypogammaglobulinemia. In such cases the plasmacytoma lacks the ability to produce globulin and crowds out the normal globulin-producing elements.

The incidence of abnormal globulins as reported by three other investigators is presented in Table 2.

In an effort to correlate differences in electrophoretic mobility with other manifestations, Slater et al.,[27] studied the immunochemical behavior of β and γ myeloma fractions and concluded that γ myeloma globulins tended to precipitate more antinormal γ globulin antibody than did the β fraction. However, Korngold and Lipari[28] found immunological cross-reactivity to be unrelated to mobility.

Bence-Jones Protein

Bence-Jones protein has been one of the hallmarks of multiple myeloma. Snapper[29] stated that it is never found in conditions other than multiple myeloma. In spite of its popularity, it has been an inconstant finding. As shown in Table 3, of the 19 patients studied for Bence-Jones protein, only 5 produced this substance.

These results are in agreement with those of Glenchur,[18] who also found that only 33% of his cases produced Bence-Jones protein.

It is interesting that Bence-Jones protein from various individuals differed with respect to amino acids,[30, 31, 32] sedimentation constants, isoelectric points,[33] crystal form[34, 35] and antigenic properties.[36] Bence-Jones protein is cleared through the kidneys so rapidly that the serum level is too small for electrophoretic studies. There has been some speculation as to whether there is a positive relationship between the abnormal serum globulin and Bence-Jones protein.

It was once thought that because of its smaller molecular weight (36,000) Bence-Jones protein was a degradation product of myeloma globulin and that a positive relationship between the serum and urinary proteins was to be anticipated.[36]

Table 3

Bence-Jones Protein

Name	Glob.	B-J
A.M.	1.51	−
W.M.	1.63	+
W.W.	2.15	+
E.R.	3.52	−
B.R.	2.4	−
L.M.	3.74	−
R.S.	3.9	−
G.J.	4.08	−
J.S.	4.3	−
B.W.	4.6	−
C.G.	8.0	+
T.W.	5.35	−
L.W.	5.35	−
A.A.	6.1	+
B.B.	6.3	−
J.R.	7.02	−
H.S.	10.74	−
C.H.	18.8	+
A.L.	2.95	−
Total Cases	19	
Positive	5	26%
Negative	14	74%

Others postulated a negative relationship since the rapid synthesis and loss of Bence-Jones protein exhausted the amino acids available for the synthesis of serum protein.

However, as is evident in Table 3, Bence-Jones protein may be present or absent whether the serum globulin is high, normal or low. This is in accord with the studies of Putnam et al.,[37] who used isotopically tagged glycine and demonstrated that the synthesis of Bence-Jones protein is independent of the abnormal myeloma globulin.

Despite its unreliability, one should not discard the Bence-Jones test since its presence increases the accuracy of laboratory diagnosis. Two of the patients who had a nondiagnostic electrophoretic pattern had Bence-Jones protein in urine. In Osserman's[38] series, 13% of the cases lacked an electrophoretic diagnostic spot in the serum, but the Bence-Jones test was positive.

Discussion of Protein Variants

Perhaps the most interesting problem of multiple myeloma is concerned with the variations in the nature and quantity of the globulins. If multiple myeloma is a specific disease, the paradox of metabolic variation remains to be explained. Information derived from the study of this disease could increase the understanding of proteins in general. Since the most characteristic pattern of multiple myeloma is a large increase in γ globulin, an effort to understand this phenomenon makes it necessary to examine other conditions associated with increased globulin.

A number of such conditions follow:

1. Compensatory—following the loss of albumin.
2. Immune reactions.
3. Liver disease.
4. Neoplasms.

1. *Compensatory.* This is somewhat speculative. When there is much loss of serum albumin, an increase of globulin might be expected. This occurs in extensive burns. However, in the massive albuminuria of nephrosis both the albumin and γ globulins are depressed. Unfortunately, the problem in nephrosis is complicated by the increase in β lipoproteins.

2. *Immune Reactions.* Most of the immune bodies are gamma globulins. Hyperimmunization of experimental animals may result in gamma globulin levels as high as 2-3 grams per 100 cc.[39] The susceptibility of hypogammaglobulinemic individuals to infections is well known. Although the early response to infection is a rise in the α_2 fraction and a fall in albumin,[26,40] it is in chronic infections that the γ complex reaches high levels.

The relationship of the plasma cell to antibody production was shown by Fragraeus,[41] who demonstrated that the production of antibodies *in vitro* by tissue slices from immunized animals was proportional to the number of plasma cells. Some investigators[42] believe that all gamma globulin is antibody. However, Tiselius and Kabat[43] found that specific immunization results not only in the production of specific antibodies but also in the appearance of nonspecific gamma globulins.

The presence of gamma globulin in plasma cells was demonstrated by Coons et al.[44] by means of the fluorescent antibody technique.

A large number of organic conditions such as collagen diseases, chronic infections and others, show a nonspecific pattern characterized by a moderate decrease in albumin and β globulin and an increase in α_1, α_2 and γ fractions. The γ increase is usually impressive and is of the heterogeneous type. This increase in the γ fraction may be an expression of the immune mechanism.

3. *Liver disease,* especially cirrhosis, is associated with high globulin levels.[45] Since the liver is the site of synthesis of albumin, it has been suggested that the increase in globulin is a compensatory mechanism to maintain colloid osmotic pressure.[46] Waldenstrom[47] believes that the diminution in albumin is secondary to depletion of amino acids by the plasma cells which have a higher priority. Additional evidence for increased synthesis of globulin was offered by Havens,[48] who found that the catabolism of γ globulin is increased in cirrhosis. Moreover, increased numbers of plasma cells occur in the marrow of cirrhotic patients.[49] The nature of the stimulus is unknown but it may be an expression of the mesenchymal reaction related to fibrosis.[50]

The dysgammaglobulinemias or idiopathic hyperglobulinemias, in these cases there is a large increase in homogeneous globulin of any complex ranging from α to γ. These individuals tend to develop recurrent pulmonary infections, but show no clinical or x-ray signs of myeloma.

Smith[51] reported 13 cases with homogeneous γ peaks and referred to this condition as non-myelomatous paraproteinemia. Four other such cases were reported by Owen and Rider.[52]

Four patients with increased γ globulin were followed by Hammack et al.,[53] for 3½ years, during which time they exhibited in-

creased susceptibility to pneumonia but showed no evidence of myeloma.

4. *Malignancy of the Reticulo-Endothelial System.* Such malignancies as lymphatic leukemia often produce a decrease in γ globulin, presumably by crowding out the plasma cells. On the other hand, multiple myeloma is notoriously associated with the overproduction of globulins, especially one which migrates as a γ (50-80% of cases). In contrast to the other "nonspecific" hyperglobulinemias, this globulin is of the homogeneous type (characterized by a sharp spike). Until the introduction of electrophoresis, there was some speculation that multiple myeloma might be either an inflammatory or a collagen disease because of increased globulin. However, the homogeneity of the myeloma globulin places it apart from other conditions associated with increased globulin. It is probable that normal γ globulin producing cells (mainly plasma cells) exhibit enormous versatility in the production of protein. Teleologically, such heterogeneity of γ globulin would be anticipated since immune bodies are specific proteins. In multpile myeloma, on the other hand, one type of malignant plasma cell may produce a single protein.[31] This protein has no immunological function, hence the great susceptibility of multiple myeloma patients to infection[54, 55] despite the high levels of globulin in some patients.

It should be noted that some cases of lymphosarcoma and lymphatic leukemia may be associated with an electrophoretic pattern suggesting multiple myeloma.[13]

Studies of terminal amino acids in globulins from patients with and without multiple myeloma by Putnam[56, 57, 58] suggest that abnormal globulins probably differ structurally from normal globulins and from each other. This was also suggested by immunochemical studies.[27, 59, 60] The present consensus is that there is only a partial immunological relationship between normal and abnormal γ globulins. All abnormal γ globulins are probably different and they remain unchanged during the course of the disease.[27, 28]

Summary and Conclusions

Multiple myeloma may exhibit much clinical variability. While the disease usually terminates fatally from 6 months to 2 years after the onset of symptoms, extreme ranges of several weeks to 12 years are described.

Although the most frequent initial symptom is bone pain, especially of the spine, the disease is occasionally ushered in by excessive bleeding.

Some patients may exhibit neurologic manifestations which cannot be attributed to pressure from osseous lesions and may be due to a toxic factor in multiple myeloma.

Electrophoresis has provided a powerful diagnostic instrument in this disease, but cautious interpretation is imperative. A high, narrow spike in the gamma globulin zone is virtually conclusive evidence of multiple myeloma. Globulin concentrations may reach exceedingly high levels. While the most common abnormal protein is in the gamma fraction, α or β globulins are occasionally produced by the malignant cells. Many cases show normal patterns or hypogammaglobulinemia.

Bence-Jones protein is diagnostic when found but is unfortunately present in less than ⅓ of all cases.

Although the characteristic x-ray picture is the most frequent clue to the existence of multiple myeloma, many cases lack this helpful sign. Moreover, numerous other conditions may mimic the radiologic bone changes. A combination of x-ray surveys, marrow examinations and electrophoretic studies is therefore essential to assure highest diagnostic accuracy.

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Defensive Aspects of Biological Weapons Use*

By

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THERE have been numerous papers published in the last few years on the use of biological weapons. I do not plan to review these or to repeat here statements made elsewhere.[1,2] To avoid this, selected portions of the Army Research Program concerned with the control of infectious disease will be discussed and used as examples to illustrate the problems associated with defense against biological weapons. This consideration will be limited to personnel in uniform as a target. Further, we will be concerned mainly with dissemination of potential agents by the airborne route and physical defense, such as masks, filters, or protective shelters, is excluded.

The problem, as we see it, may be stated thus: there is an enemy capability of unknown magnitude to induce illness in varying numbers of personnel through exposure to biological agents. Whether this can be done in a predictable fashion, so as to enhance the attainment of enemy objectives, is not an essential part of the medical problem. Neither is it a medical responsibility to equate the effectiveness of biological weapons against other members of the family of weapons. However, having admitted the capability, there then logically devolves on us the requirement to be able to handle such an attack. This is really nothing more than a restatement of a basic medical responsibility under any circumstances—to recognize, control, and treat outbreaks of infectious disease no matter what may have been their method of initiation or their magnitude.

The Army Surgeon General has a demonstrated competence to handle naturally occurring outbreaks of disease in military personnel. Where deficiencies exist, he is actively engaged in a research effort to improve his capabilities.

The Surgeon General does not have a demonstrated capability to handle the very large scale outbreaks of illness that theoretically might result from the successful use of biological weapons, nor is he directly charged with the prosecution of a research program that would provide such capabilities, this latter responsibility having been assigned to the Chief Chemical Officer of the Army. Here it should be noted that the Medical Service has very definite ideas as to how such a group of infected soldiers would be handled if the problem had to be met today. There is no reason to believe that today's methods are the optimal to be anticipated and the relationship may well be similar to that between quinine and chloroquin for the control of malaria.

In late 1954 this queer divorce of the Surgeon General's operational responsibility from the supporting research effort was recognized as an anomaly, and at the request of the Chief Chemical Officer, the Surgeon General in effect became a Chemical Corps contractor, to engage in a limited research program on certain phases of medical defense, subject to annual renewal.

The Surgeon General turned to his civilian medical advisors and there was established, within the Armed Forces Epidemiological Board, a special commission to examine the problems imposed by the threat of biological weaponry. At the same time an Army Medical Unit was set up with the study of defense against such weapons as our primary mission. It was, and is, our joint opinion that definitive answers to the defensive problems posed must be obtained by direct examination in the target—men, rather than attempting to rely on a series of tenuous extrapolations from animal data.

The deliberate production of disease in

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man to obtain answers to medical problems, of course, is in no way a new procedure. In Figure 1 there is a partial listing of diseases in which this approach has been used. Those entities followed by a cross mark are studies sponsored or conducted by the Army Medical Service.

In the study of infectious disease we are concerned with the interaction of two living biological systems, the invading infectious agent and the host—man, each capable of modifying or being modified by the other. Alteration of either can materially influence the outcome. Use of biological weapons is, of course, one method of initiating this host-infectious agent interaction. I would like to use data from one of our programs to illustrate certain "facts of life" about use of biological weapons. This was a study of the disease Q fever,[3,4,5] now known to be frequently encountered throughout most of the temperate and tropical areas of the world. Epidemiologic and laboratory data suggest that the major natural source of infection is by inhalation and that a principal natural source of infectious material is domestic animals. There are numerous examples of the ability of the causative agent, *Coxiella burnetii*, to withstand adverse environmental conditions for long periods. These factors, as indicated by significant disease outbreaks in troops in Italy and Algeria, make the natural disease one of military import, and suggest that the agent might well be used for military purposes.

Smallpox#	Murine typhus#
Syphilis	Scrub typhus#
Gonorrhoea#	Q fever#
Yellow fever	Colorado tick fever
Diphtheria	Leishmaniasis
Malaria#	Chancroid#
Typhoid#	Dengue#
Trench fever#	Sand fly fever#
Infectious hepatitis#	Brucellosis
Serum hepatitis#	Tularemia#
Tuberculosis	Relapsing fever
Amebiasis	Bartonellosis
Salmonellosis#	Cholera
Shigellosis#	Common cold
Scarlet fever	Yaws
Whooping cough	Rat-bite fever
Leptospirosis#	Lymphogranuloma inguinale
Trypanosomiasis	West Nile virus
Herpes	Lymphocytic chorio-meningitis
Measles	
Mumps	Trachoma
Rubella	Atypical pneumonia#
Influenza#	Hemorrhagic fever
Rift Valley fever	Boutonneuse fever
Schistosomiasis	Cancer
Epidemic typhus#	Plague
Psittacosis	Adeno fever

FIG. 1. Diseases which have been deliberately produced in man.

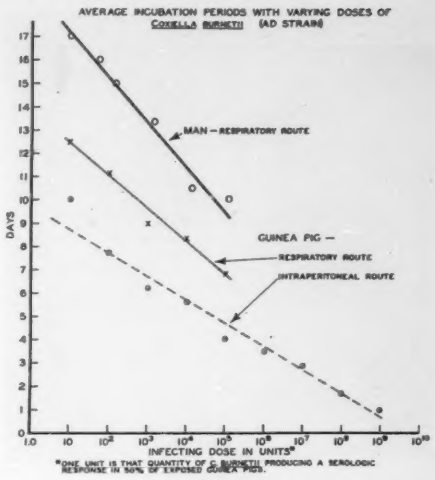
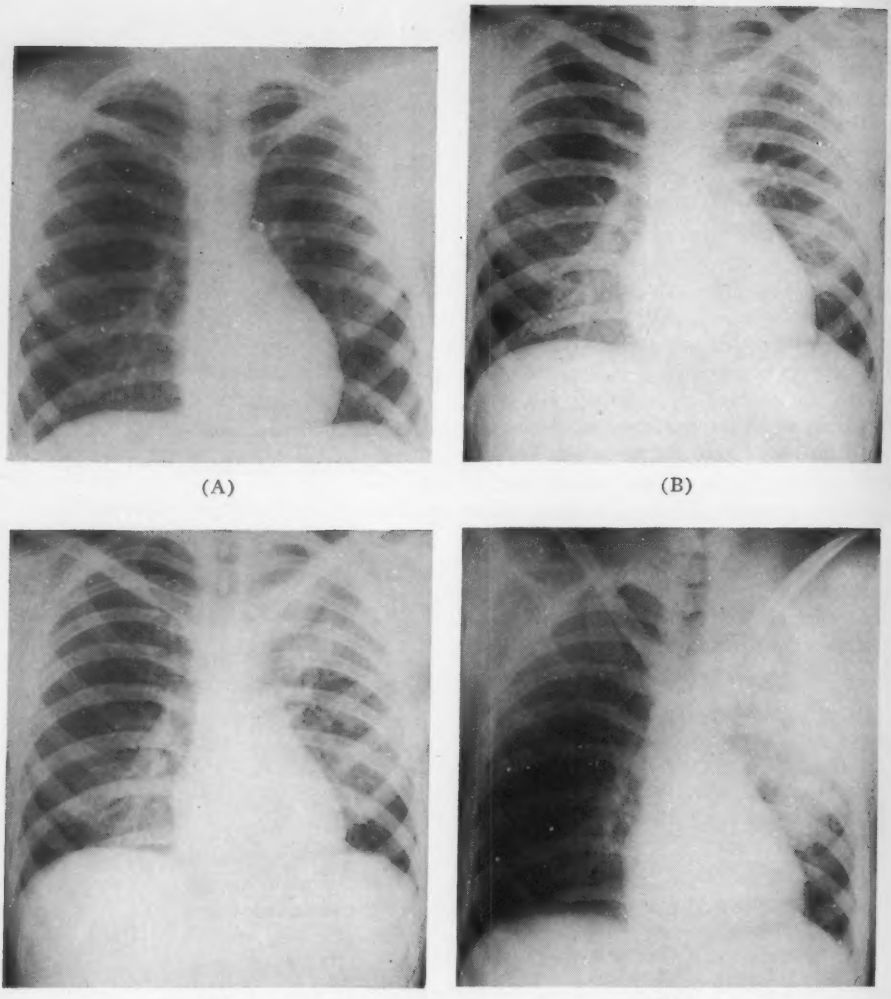

AVERAGE INCUBATION PERIODS WITH VARYING DOSES OF COXIELLA BURNETII (AD STRAIN)
MAN — RESPIRATORY ROUTE
GUINEA PIG —
RESPIRATORY ROUTE
INTRAPERITONEAL ROUTE
DAYS
INFECTING DOSE IN UNITS*
*ONE UNIT IS THAT QUANTITY OF C. BURNETII PRODUCING A SEROLOGIC RESPONSE IN 50% OF EXPOSED GUINEA PIGS.

FIG. 2. Incubation period with respect to size of inhaled dose of *Coxiella burnetii*.

After a long series of studies in animals, young adult male volunteers were exposed in groups to this agent. Every effort was made to simulate field conditions. Each man inhaled a 10 liter sample from an aerosol of whole egg slurry containing *C. burnetii*. The size dose per group was varied by dilution of the infected material with non-infected egg slurry prior to aerosolization. Other exposure factors were held constant.

These men were then observed until disease appeared as manifested by the onset of a persistent temperature above 100°F. The average length of this lag period per group, with respect to size of inhaled dose, is shown in Fig. 2. The number of infectious units inhaled is plotted along the abscissa as exponent to the base of 10. On the other axis, plotted arithmetically, is time in days. At minimal infecting doses (a very few organ-



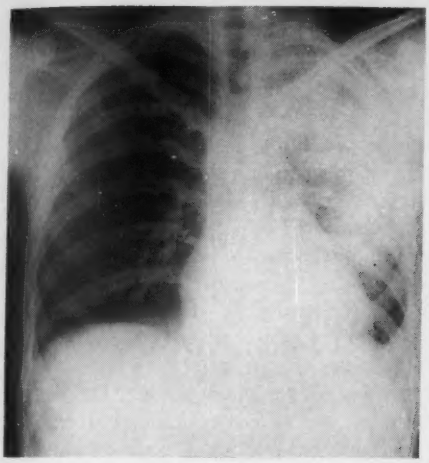
(A) (B)

(C) (D)

FIG. 3. X-rays from a case of accidental laboratory-acquired pneumonic plague. Effectiveness of early use of broad spectrum antibiotic. (A) X-ray of chest taken on induction into service. (B) Film on entry to hospital; illness twelve hours. (C) Film six hours after antibiotic started. (D) Film 24 hours after onset of illness. (Fever subsiding)

isms) the lag period in man was 17 days. With larger doses a progressive shortening of this lag time was observed, so that a 15,000-fold increase in the size of the infecting dose reduced the incubation period by almost 50 percent. Results obtained in guinea pigs by respiratory exposure or by intraperitoneal infection show a similar linear relationship.

Regardless of the size of the infecting dose, the initial phase of the disease in man was comparable to that described for natural infections in this age group. Within 24 hours after the onset of persistent fever treatment with the broad spectrum drug, oxytetracycline, was initiated. This resulted in the complete disappearance of symptoms in 24-48



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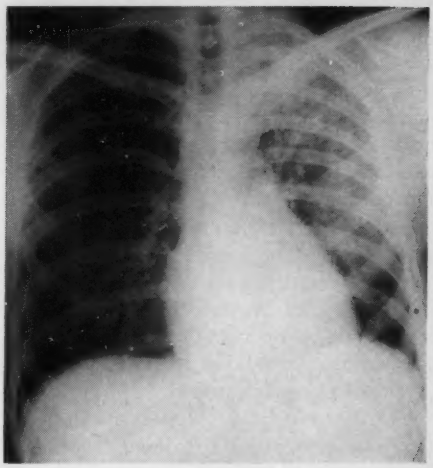

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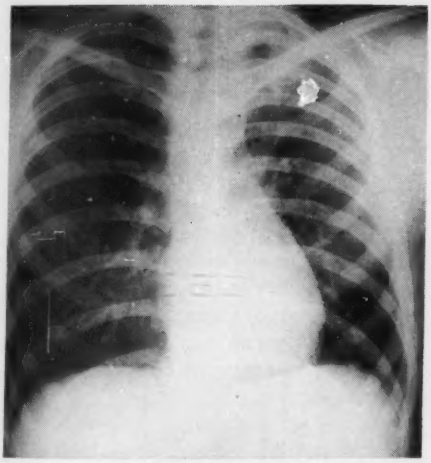

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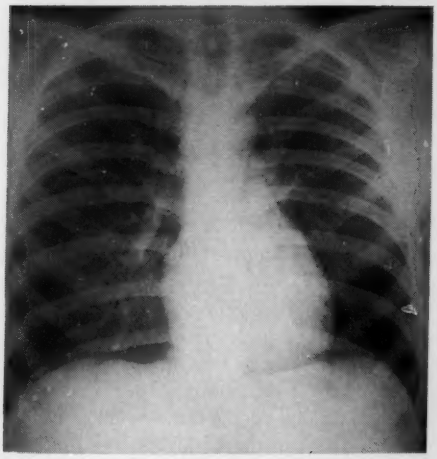

(H)

FIG. 3 (*Continued*). (E) Film taken on third day of hospitalization. (F) Film taken on fifth day of hospitalization. (G-H) Films taken on tenth day of hospitalization and on thirtieth day after onset.

hours. It was also found that this same drug, always given by mouth, would prevent or abort clinical evidence of disease if given late in the lag period. Men who had been previously vaccinated were completely immune even when subjected to very large challenge doses of the infectious agent.

This dose response and the demonstrated capability to prevent or control the disease made it possible to plan for an exposure of military volunteer test subjects under field conditions. This field trial had two primary aims:

1. To ascertain whether or not the several laboratory studies could be considered valid in terms of exposure under field conditions, and,

2. To determine whether troops could be exposed to a predicted agent concentration.

A series of preliminary field tests provided

data upon which an expected dose could be calculated. To make the test more stringent, a low dosage was deliberately planned, aiming for a human exposure of about 150 infectious units. Volunteers were then exposed in the field to an aerosol originating approximately one-half mile from them. The pattern of infection, and in particular the length of the lag period between exposure and onset of disease, was identical to that predicted, thereby strengthening the belief that the various laboratory studies on this particular disease agent could be used as a basis for conclusions which would be valid in terms of actual exposure of troops in the field.

Turning now from this specific example to our total capabilities for defense against a variety of possible biological agents, it is convenient to consider three main headings:

The first obvious method of modifying the man-infectious agent interaction is by treatment after the onset of illness. It has been shown that practically all diseases due to bacteria and rickettsia, as well as to certain of the viruses, can be controlled readily after their onset by the *early use of adequate quantities of antibiotics given by mouth.* In many instances hospitalization under any circumstances is not an absolute requirement and is certainly unrealistic under the circumstances visualized in this briefing. Please let me emphasize the term "adequate quantities" of antibiotics. One ton of today's broad spectrum antibiotics will provide one course of treatment for 45,000 people one time. The output of such drugs in the United States for 1957 was 443 tons.[6]

Adequate stockpiles of these drugs are attainable and constitute the best single move that can be made to significantly reduce the impact of bacterial and rickettsial diseases regardless of how the outbreaks may be initiated. Currently the supply requirements for these drugs are being raised to 25 grams per soldier, to be stored as close to him as feasible. This is an upward adjustment over existing Army levels of perhaps three-fold.

I have said that today's drugs are effective when employed properly. In certain diseases this is *early*—and early is measured in hours after the onset of illness. I would like to show you a series of chest x-ray films from a recent accidental case of laboratory-acquired pneumonic plague. For a baseline, the first slide shows this soldier's induction film. Please watch the left infraclavicular area. Here is his film on entry to the hospital with an illness of twelve hours duration. There is some increased density here in the lung field, which together with his clinical picture, was enough to cause us to start intensive treatment. The next slide, six hours later, shows an unmistakable change, and the following film, taken 24 hours after the onset of illness, provides ample confirmation. Despite the progress in roentgen evidence of infection, at this time his fever was dropping and he was in no distress. Here is the picture on day 3, and by this time there were no other signs of illness. Next is day 5, and finally day 10 which shows almost complete clearing. (Fig. 3A-G) With prompt and energetic drug treatment a disease with an untreated fatality rate of upward of 95 percent was promptly halted. Based on experience gained in Madagascar with naturally occurring pneumonic plague, this man would have died if treatment had not been started within 24 hours of the onset of his illness.[7] These films emphasize the capabilities and the limitations of our current methods of treatment. This is perhaps the most extreme example I could have chosen, and time is not so critical in many infections.

A second point of obvious concern revolves about the possible value of drugs begun during the lag period between exposure and onset of illness. In Q fever studies mentioned earlier this was completely successful. As a general statement, illness of bacterial or rickettsial origin may be prevented or deferred by the timely use of the broad spectrum drugs. For those infections which are not completely aborted, the onset of overt disease can be delayed so long as drug administration is continued. If disease appears after termination of prophylactic drug, reinitiation of the same drug is effective as treatment. Present day broad spectrum antibiotics have to be given every six to eight hours. Some now in

commercial development give promise of changing this time interval to twice, or perhaps once, per day.[8]

Up to this point the method of influencing the man-infectious agent interaction has been directed toward suppression of the infectious agent. We may now note some of the effects of modifying the man. It is well known to all that recovery from clinical disease due to certain infectious agents provides protection against subsequent occurrence of that disease. A similar type of protection can be deliberately obtained through the use of certain vaccines. This is the only method available to us for handling many of the virus infections since antibiotics are of no value for either prevention or treatment. Happily, for the two most serious diseases in this category, smallpox and yellow fever, excellent vaccines of known protective value are available. In both the effect is achieved by the introduction of live, but modified virus, which produces a symptomless disease. This leaves the individual protected against subsequent encounters with the fully virulent disease agent to a degree rarely obtained when dead immunizing agents are used. As a result, there is considerable interest in the development of such products.

We are fairly well along at this time in a study of such a living vaccine for the bacterial disease, tularemia. To be honest, I must tell you that this vaccine was developed in Russia and is used there on a broad scale.[9] Naturally occurring tularemia is a major public health problem for them. We now have a series of studies which unequivocally show that under optimal laboratory conditions of exposure, the infectious dose of the American tularemia organism for man by inhalation is in the order of 10 cells.[10] At this dose level the incubation period is five days. Exposure of man to 25,000 cells reduces this lag period by one-half.[11] Figure 4 shows a portion of these studies. Please note that at the several dose levels all controls became ill, and all but one required prompt treatment to control their disease. The second part of the figure shows disease incidence in men who had received the living tularemia vaccine a year prior to exposure in this protocol. Of the six vaccinates inhaling 350 cells, only one became ill and he did not require drug treatment. The same ratio holds at 1,500 cells. At the 25,000 cell challenge all vaccinates became ill and one required treatment. We, of course, do not know in volunteers what the course of the disease would be if untreated. However, in naturally occurring cases of respiratory tularemia the untreated disease, if not fatal, lasts for 3-5 weeks and is completely disabling. The untreated disease in the vaccinated volunteers at the 350 and 1,500 cell exposure levels was of 1-2 days duration and was not rated as being even incapacitating. At the very large challenge of 25,000 cells, illness lasted for two or three days and was mild except for the one man who required treatment. With treatment he was afebrile in four days. I would like to emphasize that these men had received only a single dose of the living vaccine, and that a year prior to exposure.

Exposure Dose (nominal)	Controls—Unvaccinated		Vaccinates	
	No. ill / No. exposed	No. treated / No. ill	No. ill / No. exposed	No. treated / No. ill
350	2/2	2/2	1/6	0/1
1,500	2/2	2/2	2/5	0/2
25,000	2/2	1/2	3/3	1/3

FIG. 4. Summary of exposures of volunteers immunized with viable *Pasteurella tularensis* vaccine.

We have under study at present a deliberately modified derivative of the virus of Venezuelan equine encephalomyelitis for eventual use as a vaccine.[12] This agent was chosen as a prototype for study because the infectious dose for man by the respiratory route is believed to be very small, on the basis of numerous accidental infections. The modified virus product causes a solid immunity in all test animals, and the initial studies in man appear promising. It is too early yet to make any more definite statements. Various other vaccines of this sort are under examination in laboratories throughout the world, and usable

vaccination procedures will probably be forthcoming for a large variety of specific diseases. It is to be emphasized that such vaccines must be used prior to exposure and that there may be some hazard associated with their employment. In addition, at times men so vaccinated are not fully protected and the result may be only to modify the severity of disease, or to make such a disease more amenable to treatment.

This much seems certain. As more information is gained on those factors which will result in increased virulence and infectivity of various biological agents, the same principles can be employed in a reverse manner to produce strains which are attenuated and which can be employed as vaccines to protect.

Thus far I have considered only the classical methods of disease control, since it seemed appropriate to limit this discussion to known attainable capabilities. However, information is developing to suggest that a variety of other approaches may be useful. These consist in temporary modifications of the target—man, in such a way as to increase his tolerance to disease agents. The compound, cortisone, a steroid known for its capability to control certain forms of rheumatic arthritis, is one such example. Studies now completed indicate that it, as well as other drugs, acting in a non-specific fashion will alter, under certain conditions, man-infectious agent interaction in a favorable manner. The field is new and largely unexplored, but it is our belief that at future meetings such considerations will occupy a larger and larger part of the presentations. Actually we know little, as yet, about what constitutes disease in contrast to health. It is clear, however, that infection and non-effectiveness are not synonymous, and that the outcome of a man-infectious agent interaction is subject to modifications by a variety of factors.

New modifying factors will probably be introduced in the future. At present, for many vaccines and antibiotics, we can speak with assurance concerning their capacity to control or prevent certain diseases. One particularly somber note is in order. These capabilities are valid only in terms of our present environment. What even natural disease problems may be, if we are forced to live for periods of time in areas of low radioactivity, is sheer speculation. Thus, this particular environmental factor must, sooner or later, be superimposed on our experimental studies.

In summary, we believe that we know now in considerable detail the type of medical research program which must be undertaken, if a known satisfactory capability for defense against biological weapons is to be attained and maintained. This program is hazardous, time consuming, and must inevitably involve deliberate risk to humans. It has one real bonus value, however, if properly conducted. The results obtained will be applicable to the control of disease, whether or not use of biological weapons ever becomes a reality.

Even with the serious deficiencies noted, we are firmly of the opinion that there are means currently known to materially counter the effects of a biological weapon attack against our military forces. In defense against infectious disease, deliberately induced or not, the lag period between initiation of infection and the onset of illness provides us with the opportunity for evasive action after the fact, an opportunity which is not present in other weapons systems. It is obvious that if we are to exploit this lag period there is a price in research and in logistics to be paid.

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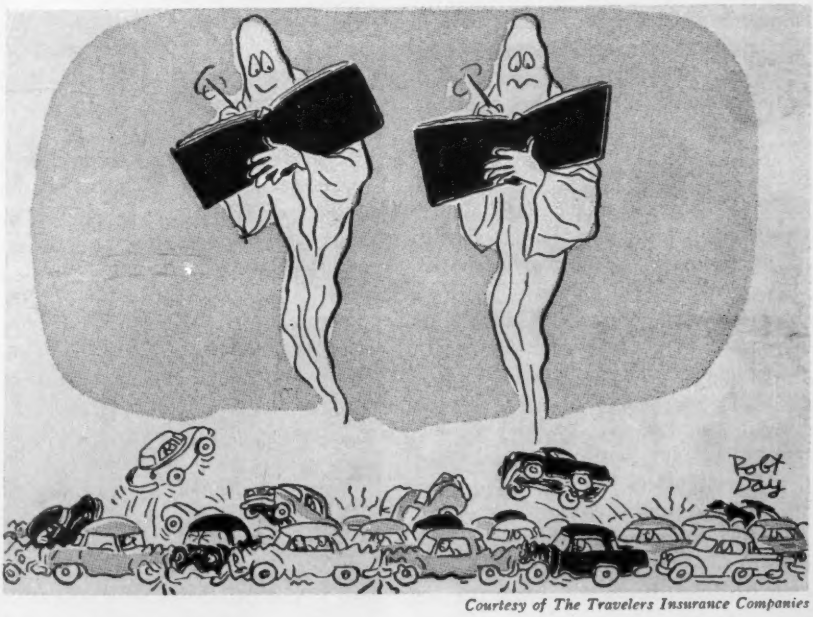
THE DEADLY RECKONING OF 1960



Courtesy of The Travelers Insurance Companies

38,000 Deaths—400 More Than 1959
3,078,000 Injuries—208,000 More Than 1959
263,100 Pedestrian Casualties—5% More Than 1959
More Than 1,000,000 Casualties From Speeding
14,900 Deaths Occurred on Weekends—Almost 40% of The Total
More Than 34% of The Drivers Involved in Fatal Accidents Were Under 25 or Over 65 Years of Age.
Almost 84% of The Casualties Occurred When The Weather Was Clear.
More Than 95% of The Vehicles Involved Were in Apparently Good Condition.
Saturday Was The Most Dangerous Day of The Week.

Surgical Aspects of Amebiasis

By

CAPTAIN LESTER F. WILLIAMS, MC, USAF; CAPTAIN WILLIAM F. QUIGLEY, MC, USA; CAPTAIN THOMAS M. GEER, MC, USA; COLONEL CARL W. HUGHES, MC, USA; AND COLONEL WARNER F. BOWERS, MC, USA

INTRODUCTION

AMEBIASIS is a common disease[9, 22] yet the disease seldom requires surgical therapy. Many patients who *apparently* require a surgical procedure can be treated adequately by medical means if the specific diagnosis of amebiasis can be made[25] and still others require surgical therapy in addition to medication;[5, 20, 25] thus, the surgeon must be aware of the protean manifestations of amebiasis. A review of the cases of amebiasis seen at Tripler U. S. Army Hospital is made and the cases with a surgical implication are discussed. During the years 1957 through 1959, those covered by this study, the Medical Service treated 20 in-patients with acute amebic dysentery.

CASE REPORTS

Case 1. A 47-year-old male was admitted with a one-month history of diarrhea consisting of 10 to 15 watery mucoid stools per day, associated with a 20-pound weight loss, easy fatigability and anorexia. The onset of this illness had occurred while the patient was in the Philippines. The remainder of the history was non-contributory.

Physical examination revealed a chronically ill patient with non-localized abdominal pain. Five centimeters from the anal orifice, a large encircling intra-rectal mass was felt.

Laboratory studies were normal except for a white blood count of 21,600 with 77 per cent neutrophils. Stools were negative for ova or parasites. Barium enema (Figure 1A) revealed a marked deformity of the rectum extending a distance of 9 centimeters and thought to be carcinoma.

An admitting diagnosis of amebiasis was made but on proctoscopic examination a "typical rectal carcinoma" was seen. Multiple smears for ameba were negative. Several biopsies were obtained. Surgery was being considered for adenocarcinoma of the rectum but was delayed because all biopsies revealed only inflammation. On one of the repeat biopsies, amebae were found.

Medical therapy was carried out with complete healing of the inflammatory mass. Barium enema after two months' therapy was normal (Figure 1B), as was proctoscopic examination.

Case 2. A 29-year-old female was admitted because of recurrent pelvic inflammatory disease. The remainder of history was unremarkable.

Physical examination was normal except for evidence of acute inflammatory disease within the right pelvis.

Laboratory studies were normal. Subsequent stools were negative for ova and parasites.

Because an ectopic pregnancy strongly was considered, an exploratory laparotomy was performed with the findings of bilateral hydrosalpinx. After a total abdominal hysterectomy was completed, a large firm mass was found in the area of the cecum. Upon finding an indurated, ulcerated area in the posterior cecal wall near the ileocecal valve, an ileotransverse colostomy was accomplished.

On subsequent study, amebic trophozoites were found within the cecal mass. Medical treatment was accomplished during the postoperative period with excellent results.

Case 3. A 27-year-old Korean sailor was admitted with a ten-day history of right lower quadrant pain after having received penicillin for the seven days prior to admission. An appendectomy had been performed in Korea 11 months prior to admission. The

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remainder of the history was non-contributory.

Physical examination revealed a 5 x 8 centimeter tender mass in the right lower quadrant below the appendectomy scar. There were no other positive physical findings.

Laboratory studies were normal except for a persistent eosinophilia. Stools were negative for ova and parasites. Barium enema revealed an extrinsic lesion distorting the cecum.

The mass partly subsided without specific therapy only to recur after one month of hospitalization. Penicillin and streptomycin were given without major change in the size of the mass.

Exploratory laparotomy was accomplished for diagnostic purposes with abscess secondary to appendicitis in an appendical stump and ameboma being considered as the preoperative possibilities. Since an inflammatory mass consistent with an ameboma was found within the wall of the cecum, the postoperative therapy consisted of terramycin and emetine. No resection was done. The mass subsequently subsided.

Case 4. A 38-year-old Malayan male was admitted with a two-day history of crampy, right upper quadrant pain. The remainder of the history was unremarkable.

Physical examination revealed only mild tenderness in the right upper quadrant.

FIG. 1A. *Case 1.* Barium enema reveals irregular fixed mass of the rectum extending 9 cm., thought by X-ray Department to be typical carcinoma.

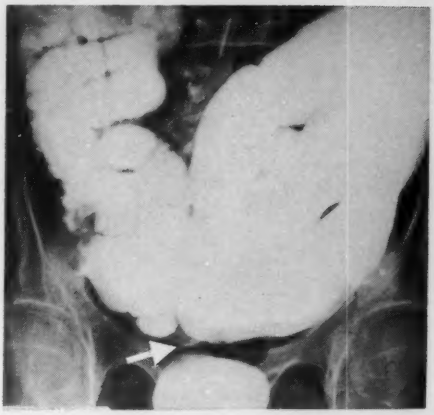

FIG. 1B. *Case 1.* Barium enema after two months of medical therapy reveals complete healing (arrow).

Laboratory studies were unremarkable. Subsequent stool examinations were negative for ova and parasites.

The patient was initially treated for biliary colic with good response. On the third hospital day, the patient became febrile. By the fifth day, there was marked right lower quadrant tenderness and the fever persisted. A diagnosis of appendicitis was made and appendectomy carried out. Since exudate from the upper abdomen was present, further exploration was accomplished with identification of a soft cystic area 6 inches from the inferior margin of the liver on its lateral diaphragmatic surface. An abscess was drained with Penrose drains and catheters. The brown thick material from the abscess subsequently was found to contain ameba.

Postoperative medical treatment was accomplished with good results.

Case 5. A 36-year-old male was admitted with a two-day history of right upper quadrant pain associated with fever. His past history was unremarkable except for episodes of chronic recurrent pancreatitis.

Physical examination revealed a temperature of 101.4 degrees Fahrenheit, right upper quadrant tenderness and a questionable right upper quadrant mass.

Laboratory studies included white blood

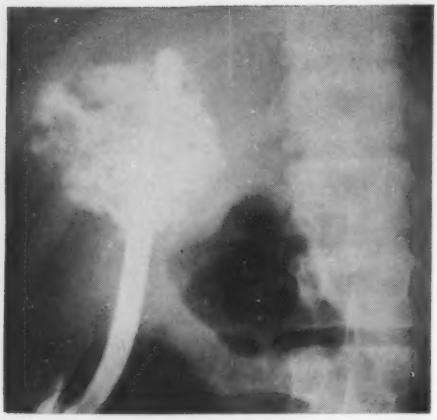

FIG. 2. *Case 5.* Amebic liver abscess; catheter placed at the time of surgery is within the abscess, the size of which is apparent. Daily irrigations of a solution containing emetine in saline were carried out.

count of 23,800 with 81 per cent neutrophils. The liver function studies were normal. A normal gall-bladder was demonstrated with an intravenous cholangiogram.

The patient was treated with nasogastric suction, intravenous fluids and antibiotics with subjective improvement. His subsequent course was marked by low-grade fever and recurrent episodes of mild pain. One month after admission, an exploratory laparotomy was performed with a preoperative diagnosis of liver abscess. On the anterolateral inferior aspect of the right lobe of the liver, an abscess containing approximately 1,000 cc. of brown thick material was found and drained.

A clinical diagnosis of amebic liver abscess was made although amebae were never demonstrated. Medical treatment was coupled with irrigation to the cavity through a catheter left at the time of drainage. Figure 2 shows the size of the cavity early in the treatment. Figure 3 shows the residual tract after therapy.

The patient has had no recurrent difficulties from the liver abscess although he has required extensive therapy for chronic recurrent pancreatitis.

Case 6. A 35-year-old male was admitted with a three-week history of abdominal pain poorly localized but mostly in the left lower quadrant. There had been a 16-pound weight loss and mild fever. The remainder of the history was unremarkable.

Physical examination revealed abdominal distention, mild left lower abdominal tenderness without a mass and evidence of a left lower lobe pneumonia.

FIG. 3. *Case 5.* The abscess cavity is markedly decreased in size. The sinus tract subsequently healed without difficulty. There was no evidence of skin infection at any time.

FIG. 4A. *Case 6.* This shows the downward displacement of the stomach by the subphrenic abscess containing multiple air fluid levels. The level of the diaphragm is not well seen but was at the upper margin of the reproduction.

Laboratory studies revealed a white blood count of 25,600 with 91 per cent neutrophils. Total bilirubin was 6.5 milligrams per cent with a direct of 3.2 milligrams per cent. There was no other evidence of liver dysfunction on laboratory basis.

The patient was treated with antibiotics for pneumonia and nasogastric suction for the associated adynamic ileus. He remained febrile. On the fourth hospital day, a questionable epigastric mass was found. Thoracentesis confirmed the presence of left pleural effusion when 350 cc. of "bloody purulent" fluid was removed. On the fifth hospital day, a diagnosis of left subdiaphragmatic abscess was made and the patient was transferred to the Surgical Service.

On review of the clinical course including the X-rays and the "bloody purulent" fluid, a diagnosis of amebic abscess of the left lobe of the liver with rupture and left subdiaphragmatic abscess was made. Therapy with chloroquine and terramycin was undertaken with subjectively prompt improvement and eventual complete clearing (Figures 4A & B; 5 and 6). Surgical drainage was not required.

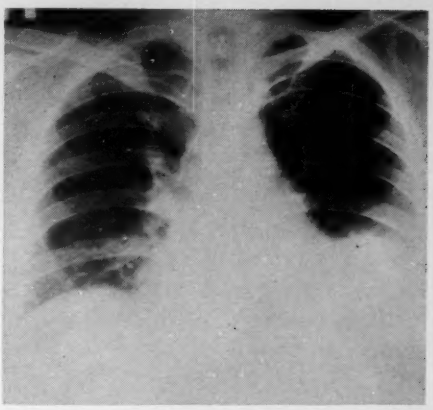

FIG. 5. *Case 6.* The chest X-ray reveals the left pleural effusion present at the time Figure 4A was obtained.

DISCUSSION

Although estimates of the population of the United States affected by amebiasis range from 4 to 20 per cent with an average of 10 per cent[9,22] the true incidence remains unknown since patients with a positive stool examination may be asymptomatic. The problem is further complicated because 50 per cent of the patients whose stools reveal parasites are infected with more than one parasite.[9] In addition the majority of the patients with complications from amebiasis requiring surgical attention, do not have Endamoeba histolytica cysts in the stool, as was true in our series.

The capsule of Endamoeba histolytica cysts which are ingested with contaminated

FIG. 4B. *Case 6.* This shows complete resolution of the abscess after medical therapy.

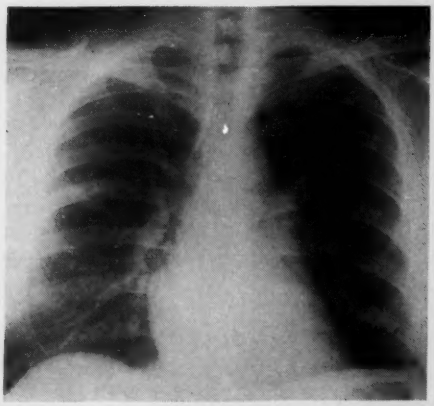

FIG. 6. *Case 6.* Complete clearing of the effusion is noted.

food or water is dissolved by the juices of the small intestines. The liberated young amebae penetrate the mucosa of the large bowel. For these reasons amebiasis is primarily a disease of the colon where it takes one of two forms.[18, 20, 26] Acute amebic colitis is an ulcerative disease; whereas, the chronic form, ameboma, is a granulomatous disease. The amebae, after causing thrombosis of the venules and veins, invade the clot and gain access to the portal circulation from which they are filtered by the liver. This results in amebic hepatitis or amebic liver abscess. Ameba can progress beyond the liver to involve the brain or lung. Cutaneous involvement is usually secondary to surgery but can be the result of direct spread from underlying disease.[18, 20, 26]

Since the initial, as well as the most common, form of amebiasis is an acute colitis, proper therapy for most patients with this disease involves only medical measures including the anti-amebic drugs. Details as to what drugs and what doses will not be discussed in this paper. Acute fulminating amebic colitis occurs rarely but can progress to perforation in hours.[4, 20] In this instance, surgical therapy[20] is added to a vigorous medical approach. The treatment of choice is exteriorization of the perforation with a proximal diverting colostomy being a reasonable substitute when exteriorization is impossible. If the perforations are extensive and multiple, ileostomy may be required. While total colectomy might be required for severe bleeding, it is not necessary with multiple perforations as the disease is reversible if the patient survives the acute episode. During the period covered by this study, 20 patients were treated medically for acute amebic colitis; whereas, only one of the six patients requiring surgical therapy (Case 1) presented during an acute colitic phase. Perforation was not seen.

The granulomatous form of amebiasis manifest by ameboma is less frequent than acute amebic colitis but more commonly carries a surgical implication.[6, 18, 20, 26, 28] Several generalizations should be stressed prior to a discussion of the specific amebomas. All patients with an ameboma require treatment with anti-amebic drugs even if the ameboma is removed.[20] Many patients with an ameboma can be treated adequately with these drugs and will not require surgery, as Case 1. An early ameboma almost always responds to medical management but the later changes involve fibrosis so that complete resolution of the mass may not occur.[20, 26] The surgical literature stresses the high mortality and complication rate associated with surgical therapy for an ameboma without preoperative anti-amebic drugs.[15, 18, 20, 23, 26, 27, 28] This problem is more pronounced in the treatment of amebic liver abscess and will be discussed fully later. Since an ameboma often can simulate a colonic carcinoma, it is far better to resect a questionable lesion and find an ameboma than it is to overlook a carcinoma.[20]

Radke[18] in reporting 119 cases of ameboma of the intestine, presents an excellent discussion including location and associated complications. The majority of these lesions occur in the cecum and the rectum (in about equal numbers).[6, 18, 20, 26] Those in the rectum are most often confused with carcinoma as in Case 1.[6] Adequate therapy can be obtained with drugs, with surgery seldom being necessary. Those in the cecum are discovered in one of several ways: as an incidental finding during abdominal surgery (Case 2); as a mass on physical examination and X-ray during the examination of a patient with abdominal complaints (Case 3); as an unsuspected finding at the time of exploration for acute appendicitis. In all such cases drug therapy is indicated. Resection is required if carcinoma cannot be ruled out (Case 2) but is unnecessary if the diagnosis of ameboma is made (Case 3). In an occasional patient only surgical exploration can distinguish ameboma and carcinoma.

An ameboma can be associated with intestinal obstruction (31 cases), perforation (16 cases), peritonitis (9 cases), intussusception (7 cases) or hemorrhage (2 cases).[18] In each of these instances appropriate surgery is combined with medical management. We have not seen examples of these.

If the amebae spread beyond the colon,

they involve the liver, with amebic hepatitis being said to occur in 5 to 10 per cent of patients with amebiasis.[5,10,13,19] Drug therapy is all that is required if the process does not progress to abscess formation. Most of the confusion which exists relative to the place of surgery in amebiasis revolves around the proper treatment of amebic liver abscess.[1,3,7,8,10,11,12,13,14,15,16,17,20,21,23,24]

Ochsner and DeBakey reviewed the literature on amebic hepatitis and amebic liver abscess.[13] Of 5,211 autopsy cases of amebiasis, 36.6 per cent had liver abscesses; whereas, of 9,696 clinical cases of amebiasis only 4.86 per cent had liver abscesses.[13] This implies that liver involvement has a poor prognosis and also that the clinical diagnosis of liver abscess often is missed. Radke[17] reported that apparently all cases of amebiasis have liver invasion, 50 per cent have a large tender liver if the patient is carefully followed and 1 to 18 per cent develop liver abscess. Yet, only 7 of 40 cases of amebic liver abscess were diagnosed clinically.[17] The diagnosis should not be difficult when the following facts are remembered.[3,10,16,17,20,24]

1. Liver involvement with amebiasis is not unusual.[10,13]
2. Approximately 70 per cent of liver abscesses are secondary to amebiasis.[11,13,14]
3. Aspirate from the abscess is usually sterile, 85 per cent.[11,13]
4. Aspirate is usually similar to "anchovy sauce," being so characteristic that it may be considered pathognomonic.[13,23]
5. All amebic abscesses present as acute rather than chronic problems.[10]

In the three patients reported, one (Case 4) had a liver abscess discovered at surgery but not suspected preoperatively; one (Case 5) was thought to have a liver abscess but its exact nature was not determined until the time of drainage; and one (Case 6) had the diagnosis made on the basis of the "anchovy sauce" appearance of pleural aspirate, interestingly enough by the Surgical Service, prior to an operative procedure.

A preoperative diagnosis of amebic liver abscess is extremely important for several reasons. Many patients, perhaps most, can be treated adequately by medical means alone. Others will require minimal surgical therapy, such as aspiration, in addition to medical therapy.[15] A very few will require formal surgical incision and drainage; however, confusion exists even in this group. The early reports found a high mortality, 22 to 43 per cent, associated with open drainage as opposed to 3.6 to 5.6 per cent mortality with aspiration and emetine.[13,15,21,24] Incision and drainage through the peritoneal space was considered very dangerous.[8,24] Operation was particularly dangerous if accomplished prior to the institution of antiamebic drug therapy. This feature was seen most often in the surgical therapy of liver abscess but was also seen with other forms of amebiasis.[18,20,26,28] The complications included cutaneous infection, activation of amebic hepatitis or acute amebic colitis (occasionally progressing to perforation), prolonged wound healing and breakdown of suture lines.[20] We have not seen any of the above complications in our five surgically treated patients in spite of the fact that none were treated for amebiasis preoperatively. One gets the impression from the recent literature that our experience is not unusual.[23] It remains true, however, that the diagnosis should be made preoperatively but more because such a diagnosis will allow adequate medical therapy which often will preclude the need for surgery than because of the fear of postoperative complications. It is always best to drain an inflammatory process extraperitoneally if possible and amebiasis is no exception.

The pulmonary complications[2,13,19,23,27,29] of amebiasis are rare (less than 2 per cent) and most commonly the result of extension from a hepatic abscess as in Case 6, but 10 per cent of 153 cases were thought to be blood borne.[19] Proper therapy includes the aggressive therapy for amebic liver abscess plus aspiration of the pleural cavity. In rare instances surgery will subsequently be required for a lung abscess, bronchopleural fistula or chronic empyema.[27] We have not

seen pericardial or cerebral complications.[13,27]

Conclusion

Amebiasis is a common disease which usually requires medical therapy including anti-amebic drugs and which occasionally carries surgical implications but seldom requires extensive surgical procedures. Every effort should be made to diagnose this condition preoperatively since only in this manner can many unnecessary operations be prevented. Rarely, an exploratory laparotomy will be required for diagnosis. Even in these cases, resection is not always necessary; however, if carcinoma cannot be excluded, resection must be done. If amebiasis is found after an operative procedure has been done, active medical therapy is required in the immediate postoperative period. The extreme dangers encountered in the past when patients were operated upon without preoperative drug therapy are not commonly encountered at this time if good surgical judgment is combined with adequate postoperative drug therapy.

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Back Pain Following Trauma and Disease—* Prolotherapy

By

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Induced Fibro-Osteogenesis strengthens weak ligament/tendon attachments to bone.
Clinical therapy—21 years; Animal experiments—8 years.

(With five illustrations)

MUSCLE coordination, balance, sensation, sense of position, and neurovascular metabolism of skeletal tissue are in response to nerve impulses that have their origin by tension-stimulation[1] of the abundant afferent sensory nerve fibrils and tension receptors which are located within the muscle-tendon and ligament attachments to bone.[2]

The ligament/tendon fibro-osseous attachments are weakened when they do not regain their normal tensile strength following sprains and tearing of the fibers, and when the fibers are weakened by decalcification such as occurs in disease, menopause and old age.[3]

This weakness of the ligament attachment to bone has been found to be the cause of much pain, referred pain, sciatica, and decalcification during the past 21 years in the management of 1,857 patients with ligament relaxation in which the diagnosis was invariably confirmed by needling, and the fibro-osseous attachments were strengthened by induced recalcification.[4]

Weak ligament fibers stretch under normal tension and permit an abnormal tension-stimulation on the nonstretchable sensory nerve fibrils and tension receptors[5] (Fig. 1). This becomes the origin (O) of: Barrages of afferent sensory impulses (A) which cause pain and referred pain (P,RP), muscle spasm (M) and reflex efferent (E) and sympathetic (S) neurovascular disturbances of bone metabolism (reflex decalcification) (RD), and inflammation of the nerves; also barrages of antidromic impulses[5-8] (AN, AX) which cause direct neurovascular decalcification (DD), and inflammation of nerves. Decalcification weakens the bony attachments of all ligaments and tendons in the area, and they become additional sources of afferant and antidromic impulses of pain, inflammation and decalcification. It is a vicious circle.

DIAGNOSIS

Diagnosis of ligament relaxation by trigger point tenderness of specific ligament attachments to bone is confirmed by intraligamentous needling with a local anesthetic solution[3] (Fig. 2). Referred pain areas are constant and direct attention to specific ligaments. Decalcification (Fig. 3) in severe cases may be observed on x-rays in 3-4 weeks[7-9] by mottling of the bone margin and fading of the major trabecula.[4]

Kohler[10] reported degeneration of 4,5 lumbar interspinous ligaments accompanied by increased mobility in cadavers, and clinically at operation after x-rays had revealed that contrast media invaded the ligaments when injected laterally.

TREATMENT

Treatment of weak ligaments/tendons is by prolotherapy[3] (*Gr-Poles*, new cells). It is accomplished by the induced proliferation of new bone and fibrosis tissue cells which permanently strengthen the fibro-osseous attachments to bone (Fig. 3). The technic consists in injecting a combined proliferating and local anesthetic solution within the weak fibro-osseous attachment. A few drops are distributed in proximate positions while the point of the needle contacts bone.

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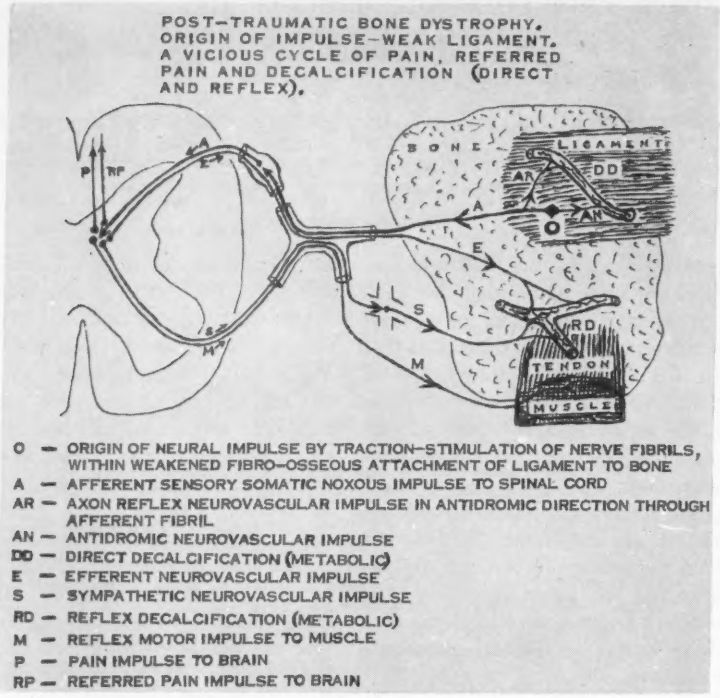

FIG. 1. Noxious Stimulation of Exaggerated Neural Response in Weak Fibro-osseous Attachment of Ligament to Bone.

Barrages of impulses *originate (O)* in an afferent somatic sensory nerve (A) when weak ligament fibers stretch under normal tension and permit *tension-stimulation* of the non-stretchable nerve fibrils within the fibro-osseous junction. Barrages of afferent impulses are transmitted (A) to the spinal cord and (P, RP) to the brain where they are interpreted as *pain* and *referred pain.*

Antidromic impulses are transmitted directly (AN) and by axon reflex (AR) to periosteal and bone blood vessels, and cause *direct decalcification* (DD) in the area of ligament attachment to bone by an imbalance of neurovascular bone metabolism.

Reflex decalcification (RD) takes place over a larger area of bone from impulses that are transmitted reflexly from the spinal cord through efferent (E) and sympathetic (S) nerves to bone blood vessels.

Muscle spasm results from reflex motor impulses (M) as a protective measure.

The new bone and fibrosis tissue cells become strong in 4-6 weeks. The patient returns for re-evaluation in 8 weeks and additional injections are given when indicated. Two proliferating solutions have been used clinically: (A)-Sylnasol (G.D. Searle & Co.) 1 part combined with 4 parts of Pontocaine 0.15% (Winthrop Lab.); (B)-Zinc Sulfate stock solution is combined with pontocaine and saline and can be prepared by any chemist.

Zinc Sulfate-Phenol Stock Solution

Zinc Sulfate	8 gms.
Liquid Phenol	12 cc.
Glycerine	24 cc.
Dist. water add to	100 cc.

Mix solution for injection as follows:

Zinc Sulfate—Phenol Stock	2 cc.
Pontocaine	42 cc.
Normal saline	42 cc.

When patients are hospitalized and comfort is assured by analgesics and sedatives,

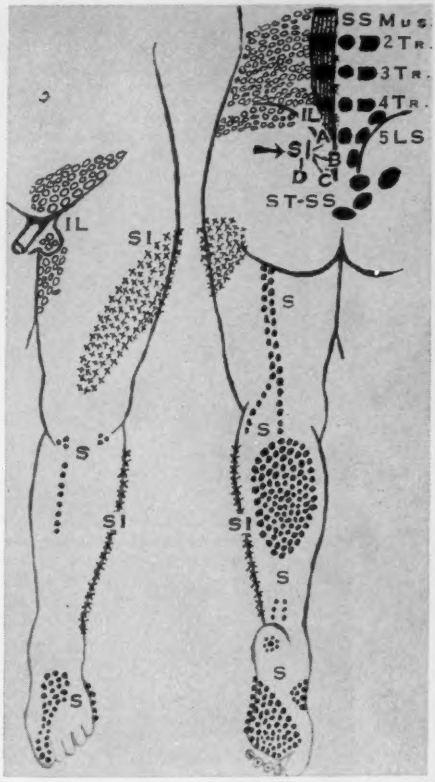

FIG. 2. Low Back Ligament and Tendon Disability.

Lumbosacral: Trigger point tenderness of the lumbar interspinous ligament (5-LS) is medial, and of the iliolumbar (IL) ligaments laterally, with referred pain into the buttock, groin, thigh, testicle, vagina, and large intestine (IL). When severe, there is accompanying trigger point tenderness of the upper portion of the relaxed posterior sacroiliac ligament (SI-A, B) with referred pain in the thigh and leg (SI). Also trigger point tenderness of the relaxed tendon attachments of the sacrospinal muscle (SS MUS) to the sacrum and transverse processes of the lumbar vertebrae, with referred pain laterally into the loin.

Sacroiliac: There is trigger point tenderness at the attachments of the relaxed posterior sacroiliac ligament (SI-A, B, C, D) and referred pain into the thigh and leg (SI). When severe, there is accompanying tenderness of relaxed sacrotuberous (ST) and sacrospinous (SS) ligaments and sciatic nerve, with pain in the area of sciatic nerve distribution (S).

Sciatica is a complication of severe relaxation of the posterior sacroiliac ligament (SIA, B, C, D), when it is accompanied by relaxation of the sacrotuberous (ST) and sacrospinous (SS) ligaments, and the tendons of the piriformis muscle, and an associated decalcification of the sacrum and ilium, and with inflammation and pain in the area of sciatic nerve distribution.

Sylnasol 1 part is diluted with saline 3 or 4 parts, thus eliminating the toxicity of the anesthetic solution so that a greater amount may be injected over larger areas. 50 cc. of Sylnasol combined with 100 cc. of saline has been used on a hospitalized patient during one treatment.

Sylnasol and Zinc Sulfate solutions have been well tolerated when adequate pre and post-treatment analgesics are given. They are devoid of systemic or allergic reactions to most patients. When such reactions occur they are usually due to the local anesthetic solution or analgesic to which the patient is susceptible.

Pontocaine provides prolonged anesthesia with a minimum of discomfort, systemic and allergic reaction, and combines readily with the proliferating agents. Some doctors prefer Xylocaine (Astra Phar.).

Male and female hormones and Vitamin C. such as Formatrix (Ayerst Lab.) and Thyroid gr., 1 or 2 daily, have appeared to materially assist in recalcification.[11, 20]

Animal Experiments

Animal experiments were started in 1952 to explain the scientific rationale for the favorable clinical results that had been obtained by strengthening weak ligaments in painful low back disability, and have been continued along with clinical observations to determine the most satisfactory combinations that would have the desirable features of: a minimum of inflammatory edema and discomfort; no impairment or destruction of any tissue; and a maximum of new bone and fibrous tissue that would become permanent.[12]

Our earlier report on animal experiments

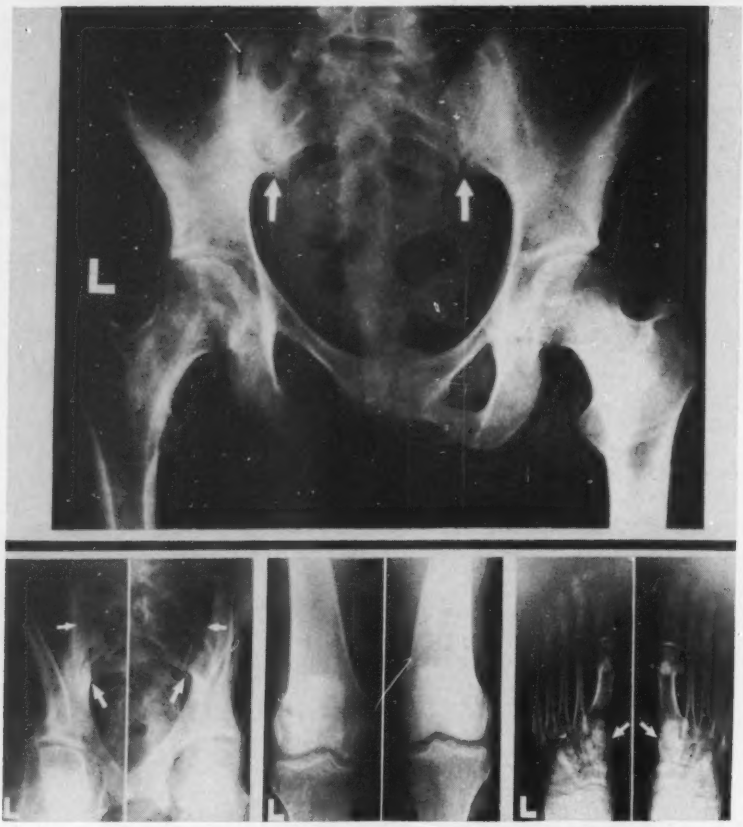

FIG. 3. Sacroiliac Ligament Relaxation, Pelvic Decalcification, Sciatica, and Recalcification

A 23-year-old nurse severely sprained the left posterior sacroiliac ligament, from which noxious bombardments of impulses caused pain and neurovascular *decalcification* of the sacrum and ilium, that relaxed the fibro-osseous attachments of the sacrotuberous and sacrospinous ligaments and the tendons of the piriformis muscle. This induced *sciatica* one month later while hospitalized in traction. Decalcification progressed throughout the left side of the pelvis and lower extremity (arrow).

Prolotherapy stimulated recalcification (arrow) of the attachments of the left sacroiliac, sacrotuberous and sacrospinous ligaments, eliminated the disabling pain, and stabilized the sacroiliac joint, so that gradual increasing activity facilitated recalcification throughout, and complete recovery.

in 1955[13] presented a history of induced fibrous tissue proliferation clinically and experimentally since 1835 when it was introduced for the treatment of hernia and later extended to include other disabilities.[14] Our report included illustrations of the induced proliferative stages from inflammation to adult bone and fibrous tissue, and tendons that had increased 40% in diameter and bone 30% in diameter, which were estimated to double tensile strength of the ligament and its bony attachment.

Schultz in 1937[15] reported 30 patients with subluxation of the temporomandibular joint that were successfully treated by injecting Sylnasol within the joint cavity. Included in the report were animal experiments in which there were no local or sys-

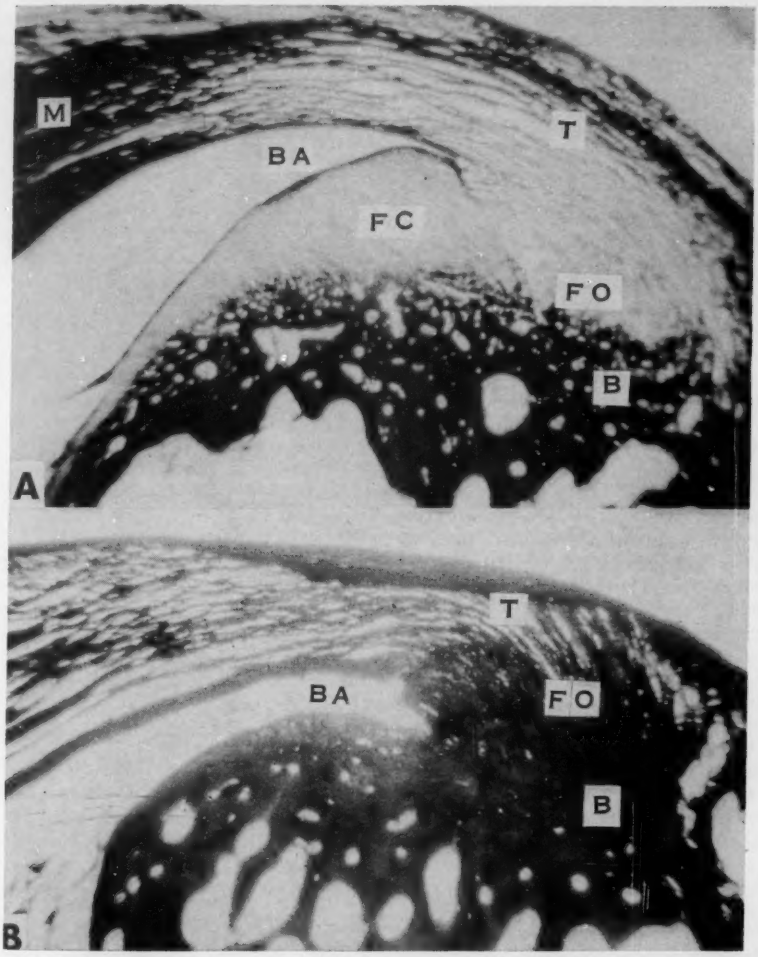

FIG. 4. Microphotographs of Induced Fibro-osseous Proliferation Bone-B, Tendon-T, Muscle-M, Fibro-osseous junction-FO, Fibro-cartilage-FC, Bursal Area-BA.

Microphotographs of decalcified Achilles tendon attachments to the tibio-tarsal bones of a rabbit, two months after 1 injection of 0.5 cc. of a proliferating solution (Sylnasol 25% in Pontocaine) was made into the right leg [B]. The injection was made against bone within the fibro-osseous attachment of the tendon. The control left leg [A] was not injected.

A. Control leg (above)

The tendon fibers (T) blend with the periosteum and continue into bone (B). They are firmly attached by calcification which extends outward into the fibro-osseous junction (FO).

B. Injected leg (below)

Proliferated new bone cells increase bone density (B), extend outward and increase the area and density of the fibro-osseous junction (FO), and encroach on the fibro-cartilage (FC) and bursal area (BA), without penetrating the tendon capsular sheath. The weld of tendon to bone is strengthened.

TABLE I

Solutions injected to determine their effect on fibro-osseous proliferation in 8 weeks following injection as compared with controls	Fibro-osseous proliferation	Early acute inflammation
1. Controls	0	0
2. Sylnasol 33% in saline (G. D. Searle & Co.)	5	4
Sylnasol 25% in Pontocaine (Winthrop Lab.)	4	4
Sylnasol 25% + Cortisone in Pontocaine	1	1–
3. Zinc sulfate (stock sol.) 4cc. in Pontocaine-saline 84cc.	5	4
Zinc sulfate (stock sol.) 3cc. in Pontocaine-saline 84cc.	4	4–
4. Sotradegol 25% in Pontocaine (Wallace-Tiernan)	2	2
5. Varisol 25% in Pontocaine (Abbott Lab.)	2	2
6. Q.U. (Plasma) 25% in Aquacaine (Farnsworth Lab.)	2–	2–
7. Salicylic acid sol. in Pontocaine (Montrose Chem.)	1	1
8. Benzyl Salicylate in oil (Bensal)	1	3
9. Whole blood (Citrated from blood bank)	1+	1–
10. Blood plasma (Citrated from blood bank)	0	0
11. Imferon (Iron Dextran, Lakeside Lab.)	0	0
12. Calcium Glucinate (Jansen-Salsbery Lab.)	1–	0
13. Estrogen, Androgen, Vit. C. (Formatrix, Ayerst Lab.)	0	0
14. Cortisone	0	0
15. Butazoladine Solution (Geigy Pharm.)	0	0
16. Silica Crystals SIO_2, in Pontocaine (Dequin Phys. Lab.)	5+	3
Silica Fluoride SIO_2, CaF_2 Pontocaine (Dequin Phys. Lab)	4+	5
Silica Oxide suspension (Abbotts)	3	2
17. Effect of daily exercise on proliferation (1 year)	1+	0
18. *Fractured tibia*—fibro-osseous proliferation in 3 weeks as compared to controls	*Callous*	Hematoma *Inflammation*
Control fracture	2	2
Sylnasol 25% (Injected at fracture site)	4	3
Zinc sulfate 4cc. (Injected at fracture site)	4+	3
Cortisone (Cortone acetate) (Injected at fracture site)	1	1
Sylnasol + Cortisone (Injected at fracture site)	2–	1+

1. One or more controls were used in each litter.

2–3. Sylnasol 1 part with Pontocaine 3 parts (25%), and Zinc sulfate stock solution—3 cc. with Pontocaine—saline 84 cc. (as used clinically) are equivalent in inducing fibro-osseous proliferation. Injections repeated at 2 month intervals induced greater proliferation than single injections.
The reactions of one year old slightly discolored solutions showed no remarkable difference than fresh solutions.
Sylnasol has been recognized as a proliferating agent of choice for 25 years[12], and Zinc sulfate has been used for 60 years[14].

4–6. Limited fibro-osteogenesis.

7–8. Inadequate fibro-osteogenesis. (Injected peri-articularly for arthritis in England.)

9–13. Whole blood stimulates fibro-osteogenesis moderately. Blood plasma, iron and calcium solutions and steroids are ineffective in stimulating fibro-osseous proliferation.

14–15. Cortisone Acetate and Hydrocortone (Upjohn) injected alone and when combined with proliferants, inhibited proliferation for 3-4 weeks and materially affected the end results following injection within tendons and at the site of fractures.

16. Various silica preparations were used. Silica Oxide crystals (SIO_2) is an excellent proliferant with only moderate early inflammation. Silica Fluoride (SIF) is effective but is accompanied by excessive early inflammation. Both precipitate rapidly causing the syringe plunger to stick. Silica Oxide suspension (Abbott Lab.) does not cause the syringe plunger to stick. (Perhaps a higher percentage of silica would be a more effective proliferant.)

17. Exercises of strain applied daily for 12 months revealed a gradual increase of fibrous proliferation and only a slight proliferation of bone as compared with the control.

18. Solutions of Sylnasol, Zinc Sulfate and Silica injected at the site of fractures (Tibia) markedly increased callous formation, over a period of 3 weeks as compared with controls, but callous was markedly inhibited when they were combined with Cortisone.
0.5 cc. of Sylnasol and Zinc Sulfate solutions injected within the tibio-talus joint induced a peri-articular inflammation. There was no sloughing but moderate limitation of motion.

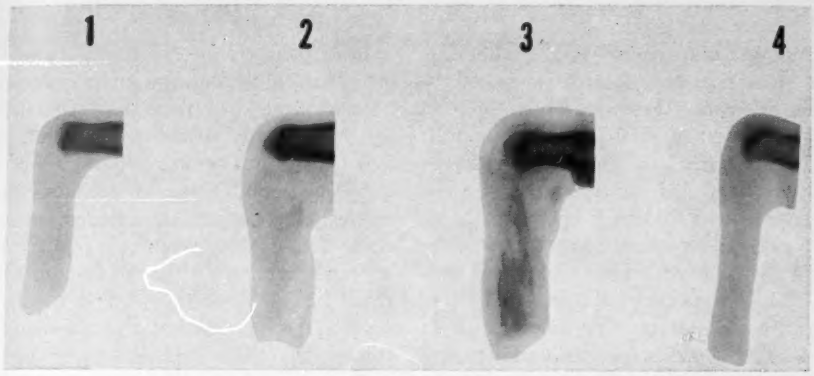

FIG. 5. X-rays of Induced Fibro-osseous Proliferation

1. Control, 2. Sylnasol, 3. Zinc sulfate, 4. Zinc sulfate + Cortisone

X-rays of the Achilles Tendon attachment to the tibio-tarsal bone of a rabbit, 1 month after 1 intraligamentous injection of 0.5 cc. of fibro-osseous proliferants.

1. Control. A faint shadow reveals bone extending into the tendons at the fibro-osseous junction where the tendon fibers enter the end of the bone and are firmly attached by ossification.

2-3. Injections of Sylnasol and Zinc sulfate solutions have stimulated the proliferation of new bone as revealed by bone enlargement and increased density, which also extends further within the tendon where ossification of the fibers strengthens the weld of tendon to bone.

4. Injection of Zinc sulfate and Cortisone solutions combined (3 to 1), reveal that Cortisone inhibited the proliferative action of the Zinc sulfate solution.

temic disturbances, infection or sloughing, following repeated injections of Sylnasol subcutaneously, and within joint, pleural, peritoneal and heart cavities. In 1956 he further reported the "soundness and efficacy" of the same treatment in several thousand patients with "lax" joint ligaments.[15]

The injection technic within tendon attachments to bone is the same as that used clinically. Experimental injections in animals were also made within joints, at the site of fractures, and intrathecally (Table 1).

One hundred ninety-two (192) New Zealand white rabbit Achilles tendons were used to determine the amount of new bone and fibrous tissue that was induced over variable periods from a few days to one year, following one or more injections of various solutions into the fibro-osseous junction of tendon to bone. The table reveals the comparative fibro-osseous proliferation that resulted over a period of 8 weeks following a single injection of 0.5 cc. of various solutions. The acute inflammatory edematous reaction following the injections are also recorded.

Intrathecal injections in rabbits of clinical intraligamentous dosage (4-5 drops) had no noticable effect. (It is further diluted by the spinal fluid.) When the dose was increased to produce spinal anesthesia, complete recovery occurred. It was necessary to use much greater then clinical dosage to induce paraplegia for a few weeks duration, which also cleared up.

The strength of the proliferating agents are so greatly diluted that 5 drops (each bone contact dose) contains only 0.01 grains of phenol crystals, and 0.017 grains of Zinc Sulfate. Further dilution would take place by mixing the 5 drops with 120 cc. of spinal fluid, should an inadvertent injection be made clinically into the spinal canal, which is impossible with our short needles used medially, and the dural sleeve of spinal nerves lying anterior to the vertebral transverse process. Withdrawal of the plunger before the injections are made against bone add additional safety.

Statistics

A number of patients (1,857) with ligament relaxation were treated by prolotherapy in 21 years. Ages were from 15 to 88 years. Duration of disability was 3 months to 65 years. They had consulted as many as 30 doctors and had undergone various unsuccessful pelvis and back operations to as many as 6 on the spine. Some had been referred to the psychiatrist. Eighty-two percent (82%) were cured to their satisfaction. There were no unfavorable sequelae. Other physicians[16–18] have reported similar success on over 11,000 patients.

Comments

Consultations with authorities on physiology, neural and vascular disorders,[5, 7–8] were valuable in evaluating our clinical and animal observations. Pain is a warning signal of noxious sensory nerve stimulation in weak ligaments/tendons, with an associated disruption of normal physiological and metabolic response. Consequently continued activities and rehabilitation exercises that cause pain are contraindicated.

Induced recalcification eliminates the noxious stimulation of neural impulses and permits gradual resumption of normal activities and reestablishment of neurovascular metabolism.

It seems apparent that extravasated blood in torn ligament/tendon attachments to bone and in fractures, mildly stimulates the proliferation of new bone and fibrous tissue cells in physiological repair. Also exercises stimulate the proliferation of fibrous tissue slowly and bone to a less degree. When disability continues, only prolotherapy will provide adequate fibro-osteogenesis. This is especially true in the loose-jointed type individual with an inadequate osteogenetic proclivity.[3, 19] The search for a silica crystal suspension that would have a minimum of acute inflammation and discomfort, and a more prolonged proliferation because of its electrolytic reaction, has not been abandoned.

Summary

Back pain occurs frequently from ligament/tendon attachments to bone that have been weakened by strain, and by decalcification of disease, menopause and old age. Weak ligament fibers stretch on normal tension and permit abnormal tension-stimulation of the abundant non-stretchable sensory nerve fibrils. This causes exaggerated afferent and antidromic neural responses that result in pain, referred pain, inflammation, sciatica, dysfunction and neurovascular dystrophy (decalcification). A vicious circle.

The diagnosis by trigger point tenderness of specific ligaments is confirmed by needling.

Treatment by induced recalcification of weak ligament attachments to bone is successful.

Experiments on rabbit tendons in conjunction with clinical observations were useful in determining the proliferating solutions and dosage to be used in prolotherapy.

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ATTEND CONFERENCE ON MEDICAL PROBLEMS AT HEADQUARTERS, FIFTH U. S. ARMY, CHICAGO

U. S. Army Photo

(*L to R*): Dr. Edwin N. Irons; Col. S. E. Dietrich, Surg. Fifth Army; Dr. Clarence W. Monroe; Lt. Col. J. W. Regan; Lt. Gen. Emerson L. Cummings, CG Fifth Army; Dr. John C. Ivins; Dr. James B. Mason; Dr. Walter G. Maddock; Dr. Frank W. Newell; Col. C. P. Ward; Dr. Harold C. Lueth; Dr. John L. Sims; Dr. Ralph E. Campbell; Dr. Paul C. Hodges; Lt. Col. W. J. Brown; Lt. Col. Nick Perlmutter.

Current Concepts in the Management of Snakebite

By

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INTRODUCTION

SNAKEBITE does not present a serious military problem in terms of morbidity or time loss. It is significant, however, from the standpoint of the morale of the personnel. A clear understanding of the preferred method for the treatment of snakebite is, therefore, important.

Unfortunately, the literature reveals varied opinions on the treatment of snakebite. This report attempts to clarify some of the concepts of treatment and is based on a review of the available clinical and experimental data. It will be confined to the treatment of pit viper envenomation since the pit viper is the family of poisonous snake most commonly encountered in this country. The copperhead, rattlesnake, and cottonmouth moccasin are all members of the pit viper family.

REVIEW AND DISCUSSION

Antivenin

In general, there is agreement that antivenin represents the definitive form of treatment for poisonous snakebite. Antivenin (Crotalidae) Polyvalent* is effective against the local and systemic effects of the venoms of all pit vipers in North and South America, and is effective against envenomation from several Asian pit vipers. Antivenin is a purified horse serum preparation containing antibodies to the venoms of the eastern diamondback (*Crotalus adamanteus*), western diamondback (*C. atrox*), and South American (*C. terrificus*) rattlesnakes, and the Fer-de-Lance (*Bothrops atrox*). Pit viper venoms are sufficiently similar so that serum containing antibodies to the venoms listed will neutralize the venoms of all pit vipers found in the geographical areas mentioned. Other antisera are available for other venoms.[1]

There are hazards to the administration of horse serum, and the use of antivenin should be reserved for cases of definite and severe envenomation, as indicated by progressing pain, swelling, and/or ecchymosis. It should be stressed that pit viper bites frequently result in insignificant envenomation and do not require specific therapy.[2-4] When antivenin is required, it should be given in adequate doses. One vial (10 cc.) may be sufficient, but 5 to 10 are sometimes necessary in serious cases.[2,4-6] The exact dose depends on the type of snake, the severity of the envenomation, and the age of the victim.[6] Children require proportionately higher doses than adults.[6]

Antivenin is most commonly administered by injecting part of the dose subcutaneously into the area of the bite and part intramuscularly at a point some distance from the bite.[4-6] In most cases this results in satisfactory neutralization of the venom.[5,6] The data of Gennaro *et al.*[7,8] indicate that the injection of antivenin into the bite area is unnecessary and that parenteral administration alone results in satisfactory protection against the local and systemic effects of pit viper venom.

In critical situations where shock, oliguria, and/or hemolytic anemia are present, the antivenin should be administered intravenously since it is maximally effective by this route.[7,9] Some observers suggest that all or part of the dose of antivenin should always be given intravenously.[6,7]

Tourniquet, Incision and Suction

The efficacy of tourniquet, incision and suction therapy (T, I&S) as a first-aid measure

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The opinions or assertions contained herein are the private ones of the writer and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large.

* Wyeth Laboratories, Marietta, Pennsylvania.

and as definitive treatment in snakebite has been questioned by many authors.[10–16] Jackson's experiments,[17–20] in which dogs injected with venom were apparently saved by this procedure, are open to criticism because only a small number of experimental animals were used, the venom dilution was not physiological, and adequate controls were not always utilized. Studies by Pope and Peterson,[21] Perry and Ya,[22] and Russell and Emery,[23] however, support his findings. In a controlled study carried out recently in this laboratory,[24] T, I&S resulted in the recovery of 22-44 per cent of injected venom *provided the incisions reached the level of venom deposition.* Essentially all recoverable venom was obtained during the first 30 minutes of suction and further suction did not yield additional venom. A delay in the onset of therapy resulted in a rapid decrease in the venom recovered, suggesting that the venom was absorbed or fixed to the tissue rapidly. After a 30-minute delay, no significant amount of venom could be recovered.

The value of T, I&S in snakebite is limited by the fact that this procedure can be destructive in itself, and the incisions make local therapy to the bitten area more complicated. Clinical data on the subject are difficult to evaluate because there is a wide variation in severity of reaction to snakebite, even among bites from large snakes. The fact that 22-44 per cent of injected venom was recovered by T, I&S in the laboratory does not indicate that the same amount could be recovered in a clinical situation where the exact site and depth of venom deposition would be difficult to determine.

Nonetheless, most authors recommend that in severe pit viper envenomation, immediate T, I&S should be carried out.[8,17–21,23–25] The tourniquet is placed proximal to the bite, sufficiently tight to occlude venous but not arterial flow, and the incisions are made through the fang marks to a subcutaneous depth. Deeper incisions will endanger vital structures and may actually hasten venom absorption if the venom has been deposited more superficially.[24] Suction should be carried out for 30 minutes. If a mechanical suction device is not available, oral suction should be performed by an individual whose mouth is free of open lesions. The victim should be immobilized as much as possible, reassured, and hastened to an area where antivenin is available and he can be followed closely by a physician. If more than 30 minutes elapse before first aid is begun, T, I&S will be ineffective and should not be used.

The wisdom of the use of this procedure by an untrained person is open to question. This is not only because of the possible harmful effects of T, I&S but also because the incisions made by an unskilled person are frequently not deep enough to effect venom removal and serve only to provide unnecessary contamination and trauma to the bitten area.

Ligature and Cryotherapy

The treatment of a bitten extremity by ligature and cryotherapy (L&C) as described by Stahnke[26] consists of the immediate application of an artery-occluding tourniquet just proximal to the bite, following which ice is placed directly on the bite area and a container of iced water prepared. The bitten limb is then immersed directly into iced water and the victim transported to a medical facility. The tourniquet is removed 10 minutes after immersion in the iced water. Continuous iced water therapy is maintained under medical supervision for 2 hours to 5 days depending on the severity of the bite, and antivenin is administered as needed for treatment of the systemic reaction. If treatment is to be continued for more than four hours, the extremity is wrapped in a plastic bag to avoid tissue trauma due to prolonged contact with the ice. Stahnke[26] emphasizes the point that the body should be kept warm enough to produce perspiration while this therapy is being carried out. He states that this will maintain circulation to the extremity and avoid the development of "immersion foot." Frostbite cannot occur because the temperature of iced water never falls below freez-

ing. The treatment of bites on the trunk is anatomically more difficult but the principle is the same.

The duration of therapy is determined by the individual case. The temperature of the water is allowed to rise gradually each day. If local pain becomes severe, it is assumed that venom is still present and active. The ice is replaced and therapy continued for another 24 hours. When gradual warming no longer produces severe pain, therapy is discontinued.

In the event that ice is not immediately available at the time of the bite, it is recommended that a small cloth pad be sprayed with ethyl chloride until frozen and then placed on the bitten area. The cloth is sprayed repeatedly as it softens. Ethyl chloride is not applied directly to the skin. This therapy is continued until iced water is available. Stahnke has designed a first-aid kit which contains an ethyl chloride spray.

The theoretical basis for L&C is that the tissue-destroying action of snake venom is related to its enzyme content and that lowering the local temperature will lower the rate of enzyme reaction and lessen tissue destruction. During cryotherapy, the skin temperature is reduced to 4-7° C. and the temperature at fang depth is 10-15° C.[26] This, according to Stahnke, almost completely inactivates the enzymes. In addition, the lowered temperature will decrease the rate of venom absorption to such an extent that the venom can be detoxified by the body as it is absorbed, with little or no systemic effect.

There are many proponents for L&C and this method of treatment has been used in a large number of clinical cases with apparent good results.[26, 27] However, evaluation of specific therapeutic procedures based on clinical impressions alone is unreliable. Disregarding the possible deleterious effects of prolonged immersion in cold water, there is very little experimental evidence supporting L&C. Stahnke[26] cites experiments carried out in cats, suggesting that L&C is effective but no controlled or statistically significant data are presented. Allen[28] has indicated that refrigeration decreases the local reaction to venom but does not affect survival.

In recent studies carried out by Perry and Ya,[22] L&C resulted in a significant delay in the absorption of venom from the site of injection but there was no improvement in survival as a result of this procedure. The local tissue destruction in the area of the bite was actually more severe than in control animals receiving venom injection and no therapy. In this experiment, L&C was not carried out in strict accordance with Stahnke's instructions since treatment was discontinued abruptly after 24 hours.

Thus the efficacy of L&C in the treatment of snakebite requires further evaluation.

Supportive Measures

Various supportive measures in the treatment of snakebite are worthy of mention and will be commented upon briefly.

Sedation. Most victims of snakebite are frightened. They should be reassured and treated with moderate doses of barbiturates as needed.[25] Morphine can be used for local pain if it is severe, although excessive doses should be avoided since there is some evidence that morphine potentiates the venom action.[26]

Tetanus antitoxin and tetanus toxoid. A snakebite represents a contaminated, penetrating wound, and the usual prophylaxis against tetanus should be carried out.

Gas gangrene antitoxin. Although there is evidence in the literature that dried venom may contain clostridia,[29] the studies of Gennaro *et al.*[8] and those of Parrish *et al.*[30] indicate that these organisms are contaminants. They were not present in the oral cavities of the snakes studied nor in freshly obtained venom. Gennaro *et al.*[8] have also shown that gas gangrene antitoxin does not alter the local necrosis produced by the injection of snake venom. Thus gas gangrene antitoxin is not indicated as a prophylactic measure in the treatment of snakebite.

Antibiotics. Parrish[30] and Gennaro[8] indicated that micrococci and coliform organisms were the predominant oral flora in the

snakes which they studied. Freshly obtained venom was sterile. Reviews of clinical cases of snakebite reveal a relatively low incidence of infection secondary to the bite.[31-33] Thus the use of antibiotics in snakebite should be limited to cases in which definite signs of infection are present or in which tissue necrosis in the bitten area is severe. When antibiotics are to be administered in the absence of definite bacteriological data, broad spectrum agents should be utilized.[30]

Antihistamine. The use of antihistamine in snakebite is based on the theory that this therapy will diminish the allergic reaction to venom and that it will counteract the effects of histamine, which some observers believe is released as a result of the action of venom on the tissues. Schottler[34] has challenged the latter theory in a study in which equivalent amounts of venom produced equal effects in guinea pigs and rabbits, despite the fact that the guinea pigs are much more sensitive to histamine. He also found that treatment with antihistamine did not alter the clinical course of mice injected with venom from South American pit vipers (*C. terrificus; B. Jararaca*). In their studies on dogs injected with western diamondback rattlesnake (*C. atrox*) venom, Parrish, Scatterday and Moore[35] suggest that promethazine hydrochloride (Phenergan) may enhance the action of the venom. Clinical studies are not available with regard to this mode of therapy. Thus a definite conclusion cannot be drawn.

ACTH and cortisone. The use of this group of compounds has been advocated on the theory that it causes an inhibition of the tissue reaction to the venom. Harris[5] suggests that ACTH and/or cortisone may block the enzymatic activity of snake venom, and Allam, Weiner and Lukens[36] suggest that they may be indicated for their antihyaluronidase effect. The clinical studies of Wood, Hoback and Green[3] and Harris[5] favor the use of ACTH and cortisone as adjunctive therapy, and the laboratory studies of Deichmann *et al.*[37] support this conclusion. However, Allam, Weiner and Lukens[36] and Schottler[34] treated experimentally envenomated animals with cortisone and hydrocortisone and demonstrated no improvement in survival.

The use of ACTH and/or cortisone may be of value as a supportive measure in cases of severe envenomation. However, the evidence is somewhat contradictory and further studies are needed for definite conclusions. The efficacy of these hormones in the treatment of serum sickness secondary to antivenin therapy is well established.

Blood transfusion. Envenomation from pit viper bite may result in hemolysis and anemia.[5] Frequent determinations of the hemoglobin and hematocrit should therefore be carried out and blood transfusions administered if needed. Blood should be crossmatched as early as possible after the bite.[25]

Conclusions

The choice of treatment for snakebite is dependent upon the individual situation. When minimal envenomation is present, reassurance and sedation are the only therapeutic measures necessary. With moderate to severe envenomation as indicated by pain and swelling beginning almost immediately after the bite, the available experimental and clinical evidence favors the following course of treatment:

1. Immobilization. The victim should lie down and remain quiet.

2. Reassurance. The victim should be reassured while treatment is being carried out. It is important to remember that the incidence of death from snakebite is low.[38]

3. Tourniquet. A venoconstricting tourniquet should be applied proximal to the bite.

4. Incision. Without delay, cruciate incisions should be made through each fang mark (or in the area of the bite if fang marks are not present). A sterile knife blade should be used if available. The incisions should be ¼- to ½-inch long and to a subcutaneous depth, usually ⅛-inch, occasionally deeper. If possible, this procedure should be carried out by a person trained in the technique.

5. Suction. Suction should be applied to the incisions in the manner described previously, and continued for 30 minutes. The

tourniquet should be released at the conclusion of the suction period.

6. Transportation. While the suction procedure is being performed, or immediately following it, the victim should be moved to an area where medical aid is available. Immobilization should be maintained while the victim is being transported.

7. Antivenin. Antivenin should be used when it is indicated and used in adequate doses; one vial may be sufficient, but as many as 10 may at times be necessary. Antivenin is not indicated when there is only minimal local reaction and there are few systemic signs. These cases will improve without treatment and the victim will be spared an unnecessary exposure to horse serum. Antivenin should be administered intramuscularly, or intravenously if the situation is critical. The usual precautions utilized in the administration of a horse serum preparation should be observed.

8. Supportive measures include sedation, tetanus booster, or tetanus antitoxin if indicated, blood transfusions if necessary, adrenal hormones for severe systemic reaction, and antibiotics for infection. A careful watch on blood pressure, urinary output, and hemoglobin and hematocrit should be maintained and the serum and urine checked frequently for evidence of hemolysis.

Summary

There is general agreement that polyvalent antivenin is effective in the treatment of pit viper envenomation, but disagreement exists in regard to other methods of therapy.

Tourniquet, incision and suction therapy (T, I&S) has been criticized by some as being ineffective. Recent work in this laboratory and elsewhere demonstrated that T, I&S begun immediately after venom injection and continued for 30 minutes resulted, under the conditions of the experiment, in recovery of a significant amount of the injected venom.

Local hypothermia (ligature and cryotherapy) appears to slow absorption of the venom from the area of the bite, but its effect on local tissue necrosis is uncertain.

Adrenal steroids, antihistamines, antibiotics, tetanus toxoid, and tetanus antitoxin may at times play a role in the treatment of snakebite. Gas gangrene antitoxin should not be used unless specifically indicated.

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"The world is hungry for what we have, not only for wealth like ours, but also for the freedom and enterprise that produced our wealth. God has sown that hunger for freedom in every human heart—and then He planted the wheat of freedom here in America and gave us hands to reap it, and make it bread for all mankind. And our work is not done, nor may we take our rest, as long as anywhere in the world a human being hungers for liberty and is not fed."—CECIL B. DE MILLE

Precipitants of Psychiatric Problems of U. S. Troops in Korea

By

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SINCE the armistice agreement of July 27, 1953, United States forces in Korea have remained in the unique position of facing an armed enemy across the 4,300 yards of no man's-land known as the DMZ (Demilitarized Zone) in a situation which is neither peace nor war, but an armed truce. For the soldiers of the combat-ready First Cavalry Division, this has meant serving a one year tour of duty under a state of constant tension, while being separated by many thousands of miles from their families in the United States. Field training and alerts are frequent, discipline rigorous, many conveniences absent, the culture unfamiliar, and the opportunities for emotional intimacy with women infrequent. After duty hours the men must remain in uniform while conditions necessitate certain restrictions being placed on their activities.

Relatively little has been written about the emotional problems of U. S. soldiers in Korea after the cease-fire. Marren[1] showed that the incidence of psychiatric disorders was greater during combat than in the months following the truce. Robbins[2] failed to find any significant differences in the emotional status of soldiers during the various phases of their tour of duty in Korea. It seemed to the author of this paper, however, that the situation in some ways was unique and called for additional consideration from a new angle.

The approach used in the study now being reported was to identify the precipitating stresses of psychiatric problems among the soldiers of the First Cavalry Division in Korea. A precipitating stress is defined as "... the immediate emotional, economic, environmental, or cultural situation which is directly related to the reaction manifest in the patient."[3] As the study was in progress, it became increasingly clear that the treatment goals of the Neuropsychiatry Clinic were to resolve the patients' acute emotional crises rather than effecting any deep-going personality changes, and that in such a setting the identification of the precipitating stress assumed great importance in the estimation of the prognosis and in the formulation of plans. It was found also that the formulation of a series of categories which divided the specific precipitants into several larger groups made it more possible to utilize the data about precipitating stress as the basis for a clinical guide to treatment and prognosis, and for the identification of areas in which preventive psychiatric measures were effective.

METHOD

Selected for this study were fifty consecutive referrals to the Neuropsychiatry Clinic of the First Cavalry Division during the months of April and May, 1959. Only those patients whose symptoms or deviant behavior significantly impaired their effectiveness were included. Most of the soldiers were referred by their dispensary physicians or commanding officers, but a few were self-referrals. These fifty patients comprised approximately 10% of the total number of patients seen at the Neuropsychiatry Clinic in one year, and seemed clearly to be a representative sample of that population.

The evaluation consisted of: (1) at least five one-hour interviews conducted by the author (the division psychiatrist), the division social work officer, and social work technicians, with all the interview material reviewed by the author; (2) the administration of an abbreviated form of the Sachs Sentence-Completion test, which was found

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to be very helpful in elucidating current stresses; (3) interviews with the patient's commanding officer, and in some cases, with the patient's chaplain, non-commissioned officers, and friends; (4) the utilization of all available additional information, such as collateral interviews which were obtained in a few instances with the patient's relatives in the United States by the Red Cross, previous psychiatric evaluations, and a perusal of the Health Records.

The decision as to what would be considered the specific precipitating stress was made by the author on the basis of his clinical judgment, after a careful review of all the available data. The most immediate and apparent situation related to the onset of the patient's symptoms was the one selected, with every attempt made to keep deeper inferences and speculations at a minimum. In most cases the patient himself cited the precipitating stress prominently in the first or second interview, while in some instances collateral interviews were necessary before the stress could be identified.

The classification of these precipitants obviously could have been done in many different ways. The method adopted here was the one that was most useful for clinical purposes, and is as follows:

Group I: *Training, discipline and restrictions.* The patient's symptoms are considered to be precipitated by (a) the rigorous field training and standards of discipline required in a combat-ready division or (b) the absence of many familiar material comforts and conveniences, or (c) the limitations placed on after duty activities. With reference to (c), throughout the division area the "off-limits" designations were widespread, while some units were located in areas where there was no civilian population or opportunity for diversion outside of military compounds.

Group II: *Job tensions.* The precipitating factor in such cases is a situation related to the patient's specific duty assignment. Three frequent sources of difficulty were settings in which possibilities for promotion appeared to be blocked, where the patient had been assigned to unfamiliar or to what for him was undesirable work, or where he had feelings of performing inadequately.

Group III: *Marital problems.* The precipitating factor is a serious deterioration in the patient's relationship with his wife. In some cases the patient's wife had stopped writing after informing him of her interest in another man, or else had suddenly notified her husband that she was suing for divorce.

Group IV: *Separation anxiety.* The symptoms appear to be precipitated by the actual physical separation from the love-object in itself, even though there is no objective reason for the patient to anticipate any weakening of the marital ties. In this study the love-object was always the patient's wife, although cases were seen outside this specific series in which it was the patient's separation from his mother that precipitated his reaction.

Group V: *Undetermined.* The precipitating factor was either so subtle that it could not be identified, or else was a situation that would have been considered to be of very little emotional significance to most other soldiers. Hence it was not regarded as relevant to the purpose of this paper, which is to define the major stresses which clearly are of importance.

Results

Table 1 shows how the fifty patients are distributed among the five major groupings of precipitating factors. Those designated as "treatment failures" are patients who were unable to complete their tour of duty with the division because they received an administrative separation or were sentenced to the stockade, or were transferred out of the theatre, or evacuated through medical channels, or as in one instance, committed suicide. The rank of the personnel and the chief symptomatic manifestation of each, and the manifestation as being delinquent behavior or anxiety and its derivatives, are indicated.

In Group I, where the major stress was the requirement of serving in a combat-

TABLE 1

PSYCHIATRIC PROBLEMS AMONG 50 U. S. SOLDIERS IN KOREA

Group	Precipitant	Total No. Patients	No. Treatment Failures	Rank			Major Symptom	
				Pvt-Corp	NCO*	CO**	Delinquency	Anxiety
I.	Training, discipline, restriction	19	11	17	2	0	14	5
II.	Job tensions	8	2	3	4	1	1	7
III.	Marital problems	7	1	3	4	0	3	4
IV.	Separation anxiety	6	0	0	6	0	1	5
V.	Undetermined	10	4	7	3	0	4	6
	Total number of patients	50	18	30	19	1	23	27

* Non-commissioned Officer
** Commissioned Officer

ready division, were 19 patients or 38% of the total, constituting the largest group and the most difficult in terms of treatment. Eleven patients or 58% of the group were treatment failures. Most of the men were privates or privates first-class, under twenty-one years of age and in the service for less than two years. They were not well motivated for military service, had little understanding of the mission of U. S. troops in Korea, were resentful that they had been assigned to serve in the area, and had little feeling of loyalty to their unit or friends. Sixteen of these patients (Table 2) were diagnosed as having personality disorders. In treatment it was important to make clear that medical channels could not be used for the purposes of secondary gain, and to appeal to the patient's enlightened self-interest in terms of the advantages of successfully completing his military career. Treatment was most successful with those soldiers whose main difficulties stemmed from limitations on their after-duty activities, and who might have made better adjustments in a rear area.

Private M., 19 years old, referred himself to the Neuropsychiatry Clinic because he had the strong desire to go AWOL from his unit, was feeling very anxious and irritable and feared he "might be going crazy." Private M. was a very self-centered and impulsive youth who enlisted in the Army "to get it over with" and deeply resented military discipline. It was apparent after two interviews that his symptoms were related to his feelings about being assigned to a very isolated unit with a heavy training schedule and far removed from any civilian population. While in his interviews with the psychiatrist he was given an opportunity to express his bitterness about his assignment and duties, and his envy of those with

TABLE 2

CLINICAL DIAGNOSIS AND PRECIPITATING STRESS OF PATIENTS IN THIS STUDY

Precipitating Stress	Personality Disorders	Neurotic Reactions	Psychotic Reactions	Psychophysiologic Disorders
I. Training, discipline, restrictions	16	2	1	—
II. Job tensions	3	5	—	—
III. Marital problems	3	4	—	—
IV. Separation anxiety	4	1	—	1
V. Undetermined	8	2	—	—
Totals	34	14	1	1

more favorable assignments, it was pointed out to him that he had not taken advantage of the week-end passes he could have obtained. It was also made very clear that there was no possibility of medical evacuation or transfer, and that going AWOL would have serious consequences for his future. He returned to the Neuropsychiatry Clinic on occasion for one or two interviews when he was particularly angry at sergeants, but he did complete his tour of duty with a satisfactory performance.

In Group II, where the problems centered about difficulties with the specific duty assignment, were 8 patients, or 16% of the total. All of the patients in this group were men who were planning to make the military service a career. They were ambitious men with good military records. Treatment was aimed at helping the patient to express and integrate his hostile feelings, and, if indicated, "indirect psychotherapy" in the form of discussions with the patient's superiors which on occasion resulted in changes in assignment. It was the observation of the author that when men are separated from their homes and families, work assumes a much greater than usual emotional significance, and symptoms related to job difficulties should be taken seriously by medical officers. One of the patients in this group was a 29-year-old master sergeant who committed suicide by hanging himself during a depression related to feelings of inadequacy in his work. If he had not been separated from his wife and four young children, the balance of psycho-dynamic forces would have been different and he might not have ended his life.

Following is a case summary of another patient from this group who was treated successfully.

Major X., who had just returned from three weeks leave, was found in his room crying and talking of suicide. When seen at the Neuropsychiatry Clinic he appeared to be in an acute neurotic depression, insisting that he was unbearably lonely for his family and had to return to them under any circumstances. Further investigation showed that although he had been performing quite satisfactorily in his job, it was a position with which he was very unfamiliar. Just prior to going on leave his commanding officer with whom he had a very close relationship had returned to the United States and the battalion was preparing for a complicated exercise. The patient was able to express his intense feelings of inadequacy in his position and his anxiety about the forthcoming field operations. His new commanding officer reassigned him to the type of work in which he felt more competent, and his depression lifted quickly as he returned to duty.

Six of the seven (14%) patients in Group III had had marital difficulties prior to their assignment to Korea, but they became more serious with the separation. The feeling of helplessness at being so far from their wives and being unable to take any action was particularly distressing. Treatment was directed towards helping to lessen the blow to the self-esteem while helping the the patient to ascertain the actual situation at home. As shown in Table 1, only one of the patients in Group III was unable to complete the tour of duty.

Sergeant B. was brought to the Neuropsychiatry Clinic and hospitalized in an acute dissociative state, barely able to walk and disoriented for time and place. He insisted that the year was 1953 and that he was home with his wife. Interviews with friends in his unit revealed that the day before he had received a letter from his wife stating that she was in love with another man and wanted a divorce. This was his wife's third marriage and she had been unfaithful to him many times during their four years of marriage. Sergeant B. was helped to overcome the narcissistic injury and to accept the reality of his wife's desertion, which had been confirmed by other sources. After several weeks he was able to return to duty and no relapse occurred.

In Group IV were six patients, or 12% of

the total, all married men and non-commissioned officers. For this group the physical separation from their wives and families in itself precipitated the emotional disturbance. These men leaned heavily on their wives for emotional support and the gratification of dependent needs, and separation evoked a great deal of anxiety related to fears of losing their wives' affection. This is in agreement with the hypothesis offered by Zehrer[4] that "those who are basically dependent persons and are separated from their families because of overseas assignment develop feelings of guilt and anxiety to a degree that it hampers efficiency and social adjustment." Three of the patients resorted to excessive alcoholic intake. There was only one patient in this group involved in delinquent activity. A relationship type of psychotherapy with the use of tranquilizers helped all of these men to complete their tour of duty without requiring evacuation or hospitalization.

Sergeant G., 39 years old, was referred to the Neuropsychiatry Clinic by his commanding officer. The sergeant's drinking was seriously interfering with his efficiency and administrative action was being considered. Sergeant G. was married to a woman eight years older than himself who treated him in a very maternal fashion, and whose love was vital to him in maintaining a sense of security. The few times they had been separated in the past, the patient would always drink excessively. As soon as he boarded ship for his overseas voyage, he became anxious and looked to alcohol for relief, and this pattern continued after he arrived in Korea. Although his wife was in good health and writing to him frequently and affectionately, he feared that somehow "things might not be the same" when he returned home. With supportive psychotherapy and the liberal use of vitamins and a tranquilizer, he completed his duty without further drinking.

For the ten patients, or 20% of the total, in Group V, the development of their symptoms was due primarily to intrapsychic emotional conflicts and had little direct relationship to either their assignment in Korea or serving in the armed forces. These patients were unmarried or divorced, had very vague and poorly defined goals in life, and were unrealistically looking to the Army for an answer to their difficulties. Three patients had re-enlisted into the Army after the age of thirty with only two or three years of previous service and after a break of at least seven years.* Eight of the ten patients were diagnosed as having personality disorders, including two with homosexual problems and one enuretic. With the six patients that were able to complete their tour of duty, treatment was directed towards suppression of symptoms.

Private J., a 36 year old divorced soldier, was referred for psychiatric consultation because of frequent visits to his medical officer for a variety of hypochondriacal complaints. Private J. was diagnosed as having a schizoid personality disorder, with a great deal of underlying resentment about serving with men much younger than himself, and with an exaggerated conception of his military capabilities. This was his second enlistment in the Army, having re-enlisted several months prior to coming to Korea after a break of seven years, and it occurred shortly after being divorced by his wife. Nothing in the current external environment could be identified as a significant precipitant of his symptoms. After his initial evaluation he refused further appointments, stopped seeing his medical officer about his physical complaints, and continued to function at a marginal level for the remainder of his tour of duty in Korea.

Table 2 shows the number of patients in the major diagnostic categories and their distribution among the five groups of pre-

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* Further experience at a general military hospital has led the author to believe that more intensive psychiatric screening of men enlisting after the age of thirty and with break in service of several years might be warranted.

TABLE 3

TREATMENT FAILURES AMONG PATIENTS WITH NEUROTIC REACTIONS AND PERSONALITY DISORDERS

Group	Neurotic Reactions		Personality Disorders	
	No. of Patients	No. Failing to Complete Tour	No. of Patients	No. Failing to Complete Tour
I	2	2	16	9
II	5	—	3	1
III	4	—	3	1
IV	1	—	4	—
V	2	—	8	4
	—	—	—	—
Totals	14	2	34	15

cipitating stresses. There were actually eighteen different specific reaction types among the fifty patients in this study.

Although establishing a clinical diagnosis is essential in the proper evaluation and treatment of patients with psychiatric disturbances, in itself it was not as useful a guide to prognosis and treatment in this setting as was the precipitating stress and its separation into one of several groups. From Table 3 it can be seen that of the sixteen patients with personality disorders in Group I, nine (56%) failed to complete their tour of duty, while the four patients with personality disorders in Group IV responded successfully to therapeutic intervention. Although the prognosis of patients with neurotic reactions was generally excellent, the two patients with this diagnosis in Group I were both treatment failures. In addition, the clinical diagnosis does not point out and focus attention on the areas and problems towards which treatment efforts must be directed as does the careful identification of the precipitating stress.

COMMENT

The ability of psychiatrists to predict accurately whether an individual will make a successful adjustment to military service has been demonstrated to have important limitations. A study by Glass and his associates[5] in evaluating the ability of six trained psychiatrists to predict the future military performance of 505 inductees revealed that although a 93% rate of accuracy was achieved in predicting effective performance, the rate of accuracy was only 24% in identifying the unsatisfactory soldier. They state: "It is this inability to determine in advance the potential below-average or poor soldier that is the basic unsolved difficulty of psychiatric selection. In general, too many individuals are considered to be of unsatisfactory caliber or of questionable value for military service." The six psychiatrists also differed significantly among themselves in their predictions, even though they used a uniform and specifically defined examination procedure.[6]

One of the reasons for this inability of psychiatrists to predict more accurately military performance is the failure to give sufficient consideration to situational factors and environmental stresses, and the lack of information about them. Psychiatrists often find themselves forecasting adjustment without consideration of what it is exactly to which the individual will be attempting to adjust, and without assessing his vulnerability to specific stresses. On the other hand, too much importance is given to the clinical diagnosis and the existence of latent psycho-pathological trends. "It should be apparent that each level of a combat theatre has its own specific situational circumstances which play a larger role in determining the over-all effectiveness of assigned personnel than previous personality characteristics or so-called predisposition."[5] Farrell and Appel,[7] in discussing the experiences of World War II state: ". . . a number

of factors were important in causing psychiatric disorders. Personality structure was merely one of several. Fatigue, leadership, morale, discipline, job assignment, motivation, training, domestic difficulties—each of these might be as important as personality structure in any given case and in combination frequently more so."

Although the importance of environmental factors is most apparent in combat situations, it does not follow that psychiatric disorders occurring during "routine military duties" are unrelated to external stresses or are the inevitable evolution of intrapsychic conflicts that would manifest themselves in any context. The problems faced by men and women in the armed forces are varied, and in many respects quite different from the challenges of civilian life, both during war and peace time.

There are many excellent analyses of the situation problems faced by servicemen in making the transition from civilian to military life, and of the characteristics of military society.[8-12] Menninger[12] has discussed the environmental stresses faced by soldiers during the training period, overseas non-combat duty, and in combat. During the training period he considers such factors as: the demands of the new life, discipline, strenuous physical demands, lack of privacy, frustrations, assignment, danger, competition, personal problems, and promotions; in overseas non-combat duty: uncertainty, separation, privation, isolation, and climate; in combat: fear, fatigue, tour of duty, and disparity of privilege. What is needed now in order to test the validity of these observations and to make them more useful clinically is to determine: (1) to what extent, if any, do these stresses contribute to precipitating psychiatric breakdown; (2) what is the relative significance and prevalence of these stresses in different areas and types of assignments; (3) who are the men who are vulnerable to each of these stresses, in terms of personality structure and traits, clinical diagnosis, rank, education, and other factors.

If this information were available, it would be useful in many ways, particularly in providing the psychiatrist with a sounder basis for making recommendations and predictions concerning assignments to particular areas or jobs, and from the standpoint of preventive psychiatry.

Summary

Since the armistice of July, 1953, U. S. troops in Korea have faced an enemy across the Demilitarized Zone in a state of armed truce, under constant tension, separated from their families in the United States. Field training has been frequent, discipline rigorous, after-duty activities restricted, and the culture unfamiliar.

The treatment goals of a Neuropsychiatry Clinic in this setting focussed on an attempt to resolve the patients' acute emotional crises rather than to effect deep-going personality changes. Under these circumstances it was found that the identification of the external precipitating stress and its categorization into one of several major groups was more useful for prognostic and treatment purposes than was the clinical diagnosis.

To determine what features of the Korean assignment contributed to the precipitation of psychiatric problems among U. S. soldiers, fifty consecutive referrals to the Neuropsychiatry Clinic of the First Cavalry Division during the months of April and May, 1959, were given a thorough clinical evaluation, including the utilization of collateral interviews. The patients were divided into five groups on the basis of the major stress that precipitated their immediate psychiatric problems, as follows: Group I, training, discipline, restrictions, nineteen patients (38%); Group II, job tensions, eight patients (16%); Group III, marital problems, seven patients (14%); Group IV, separation anxiety, six patients (12%); Group V, undetermined, ten patients (20%). Data and observations are presented concerning the prognosis, treatment and clinical features of the patients comprising each group.

The predictive ability of psychiatrists is believed to be hampered by the lack of information about, and failure to give suffi-

cient consideration to situational and environmental stresses, with consequent overemphasis of personality predisposition.

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MILITARY AIDS IN TRAINING CIVILIANS

U. S. Army Photo

Students and instructors of the Mather School of Nursing at the Southern Baptist Hospital in New Orleans don gas masks prior to testing such protective device in a temporary tear gas chamber set up at Camp Leroy Johnson, New Orleans. Members of the 394th Transportation Battalion assist in this phase of emergency and disaster nursing instruction conducted by battalion personnel.

Factors Affecting Nurse Staffing in a Federal and Non-Federal General Hospital

By
EUGENE LEVINE, PH.D.*

INTRODUCTION

THERE are now nearly a half million professional nurses in the United States.[1] In addition, another half million persons are employed as auxiliary nursing personnel. Although these may seem like large numbers, there is, nevertheless, a severe and persistent nursing shortage. In hospitals, where about sixty percent of the total professional nurse supply is employed, the shortage of nursing personnel seems to be especially severe. A recent study reported over 22,000 vacancies for professional nurses in hospitals.[2]

Solutions to the nursing shortage that have been proposed fall into two broad categories. First, there are those which are aimed at producing numerical increases in the nurse supply. Efforts to increase recruitment into schools of nursing and to attract back to the profession nurses who are inactive are examples of what can be called the quantitative solutions to the nursing shortage.

Second, there are approaches to the alleviation of the nursing shortage which can be called qualitative solutions. These are concerned with increasing the productivity of the existing nurse supply through such means as improvement in the utilization and educational preparation of nursing personnel.

The value of qualitative solutions to the problem of nursing shortage has been demonstrated by recent research findings. That some hospitals may be making more productive use of their personnel than others was suggested by a recent report of a study entitled *Effect of Nurse Staffing on Satisfactions with Nursing Care*.[3] This study attempted to measure the relationship between the size of a hospital's nursing staff and the adequacy of services provided. One of the findings was that some hospitals with smaller staffs of personnel provided services that were as adequate as hospitals with larger staffs. This finding raised an intriguing question: What are the specific factors which enable one hospital to provide as adequate nursing services as another with a smaller nursing staff? If these factors could be delineated some specific solutions to the problem of the nursing shortage might thereby be found which would not necessarily entail numerical increases in the existing supply of nursing personnel.

To attempt to answer this question, the author of this article conducted a study in three general hospitals that provided care to the same number of patients but differed in a most important way: one hospital had a much smaller nursing staff than the other two. The purpose of the study was to identify the specific factors which affected nurse staffing in the hospitals and to measure the extent to which these factors contributed to the difference in staffing between the hospitals. In other words, the main question which this study sought to answer was: Which factors present in the hospital situation enabled one hospital with a smaller nursing staff than another hospital to provide care to the same number of patients? This article will present a brief report of the method and findings of this study.

METHOD

Selection of hospitals. To select similar sized hospitals with different numbers of

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TABLE 1

RATIO OF NUMBER OF FULL-TIME NURSING PERSONNEL EMPLOYED[a] PER 100 AVERAGE DAILY PATIENT CENSUS, FEDERAL AND NON-FEDERAL GENERAL, SHORT-TERM HOSPITALS,[b] FALL, 1958

Category of personnel	Ratio of nursing personnel per 100 patients		
	Federal hospitals	U.S.P.H.S. hospitals	Non-federal hospitals
Total, all personnel	53.5	53.6	110.4
Administrative personnel	8.9	10.2	22.4
Professional nurses[c]	6.7	6.0	16.3
Other nursing personnel[d]	2.2	4.2	6.1
Bedside nursing personnel[e]	37.1	36.4	71.5
Professional staff nurses	13.0	16.4	26.8
Other nursing personnel	24.1	20.0	44.7
Other nursing care personnel[f]	7.5	7.0	16.5
Professional staff nurses	1.5	2.0	5.3
Other nursing personnel	6.0	5.0	11.2

[a] Includes an estimate of the full-time equivalent of part-time personnel.

[b] Tabulation based on 4,897 non-federal general hospitals, 386 Federal hospitals, 12 Public Health Service hospitals.

[c] Includes directors, supervisors, head nurses, instructors of inservice education, and their assistants, and nurses assigned to central supply room.

[d] Practical nurses and nursing aides assigned to central supply room and ward clerks assigned to patient care units.

[e] Nursing personnel assigned to patient care units.

[f] Nursing personnel assigned to operating room, recovery room, delivery room, emergency room, and outpatient department.

Source: Computed from data in American Hospital Association, "Guide Issue," *Hospitals, Journal of the American Hospital Association*, 33: Part 2, Tables 7 and 8, pp. 426–431, August 1, 1959.

nurse staffing, the nurse staffing patterns of the 5,300 short-term general hospitals in the United States were analyzed. Staffing data, available from the 1958 annual survey conducted by the American Hospital Association, showed two outstanding characteristics. One was the great variability among hospitals in the ratio of nursing personnel to patients. From the data it seemed that few hospitals in the United States had exactly the same nurse staffing pattern.

The other characteristic, shown in Table 1, was the large difference in the ratio of nursing personnel to patients between Federal and non-federal short-term general hospitals. In 1958, non-federal hospitals employed, on the average, twice as many nursing personnel for each patient as did Federal hospitals. This difference in nurse-patient ratios between Federal and non-federal general hospitals provided an excellent opportunity to conduct a study of factors affecting nurse staffing. Therefore, one Federal and two non-federal hospitals were selected for intensive study of the factors that might affect nurse staffing. The Federal hospital was the Public Health Service Hospital at Boston, Massachusetts. In the Fall of 1959—the period in which this study was carried out—the Public Health Service Hospital had 247 beds, an average daily census of 186 patients and a nurse-patient ratio of 49.9 personnel per 100 patients.

The two non-federal hospitals selected for study were matched to the Public Health Service Hospital in terms of two criteria: (1) size, and (2) absence of a school of nursing. Both were voluntary, community

hospitals, located in the suburban area of a large city. These hospitals had between 210 and 250 beds and an average daily patient census similar to that of the Federal hospital. The nurse-patient ratios in the non-federal hospitals were over twice that of the Federal hospital.

Factors studied. Two main questions were pursued by this study. First, which factors influence the size of the ratio of nursing personnel to patients in a general hospital? Second, to what extent do each of these factors explain why the Public Health Service Hospital was operating with 49.9 nursing personnel per 100 patients while the non-federal hospitals were operating with the much larger staffs of 113.0 and 125 personnel per 100 patients?

Three broad factors were hypothesized as explaining why the Federal hospital was operating with half as many personnel as the non-federal hospitals: workload, adequacy of services, and the organizational characteristics of the hospitals.

Workload. Since the Federal hospital employed so many fewer personnel it was hypothesized that its patients had fewer requirements for nursing services than patients in the non-federal hospital. That is to say, patients in the Federal hospital were less sick, more capable of taking care of their own needs, and less dependent on nursing personnel. This seemed like a reasonable hypothesis since for many years it has been argued that the longest average length of stay of patients in Federal hospitals is indicative of a lesser acuity of illness among Federal patients.

To measure the patients' requirements for nursing services, a classification method was applied to a representative sample of patients in the Federal and non-federal hospitals studied. This method was recently developed in Johns Hopkins Hospital under the guidance of Dr. Charles D. Flagle, Director of Operations Research.[4] Through the use of this methodology, nurses in the hospitals studied evaluated the requirements of a large sample of patients in terms of several tangible factors: (1) ambulatory status, (2) assistance needed for bathing, (3) assistance needed for feeding; and whether the patients had one or more of the following characteristics: (a) incontinent, (b) isolated, (c) unconscious, (d) marked emotional disturbance. Based on these ratings each patient was classified into one of three categories of nursing requirements: (1) intensive care, (2) intermediate care, (3) minimal care. From the distribution of patients into each of these three categories it was possible to estimate the extent to which the lower staffing in the Federal hospital was attributable to lower patients' requirements for nursing services.

Adequacy of nursing services. It was further hypothesized that if the lower staffing in the Federal hospital was not completely explained by a lower workload in this hospital, then the Federal hospital might be providing less adequate services to its patients because of its smaller workforce. Thus, a comparative study was made of the adequacy of the nursing services in the hospitals to determine to what extent the lower staffing in the Federal hospital might be related to a less adequate level of nursing services in this hospital.

To measure adequacy of nursing services, a methodology developed by the Division of Nursing Resources, Public Health Service, was used.[5] The purpose of this methodology is to assess adequacy of nursing services by measuring the frequency with which patients' requirements for nursing services are fulfilled. To determine this frequency in the hospitals studied, checklists were filled out by a sample of patients and personnel. These checklists contained fifty items which described incidents in which specific needs for nursing services were not fulfilled. The number of items checked by respondents provided a score that was a measure of the adequacy of nursing services provided.

Organizational characteristics. It was further hypothesized that if the lower staffing in the Federal hospital was not completely explained by (1) a smaller workload and (2) a lesser adequacy of services, then it must also be related to the factor of organizational

TABLE 2

FACTORS WHICH MIGHT AFFECT NURSE STAFFING IN A GENERAL HOSPITAL

I. *Workload*
As measured by patients' requirements for nursing services.

II. *Adequacy of Nursing Services*
As measured by the extent to which patients' requirements for nursing services are unfulfilled.

III. *Organizational Characteristics of the Hospital, and the Nursing Department*

A. Organizational environment—historical development, community setting, physical structure and layout, equipment and supplies, and fiscal resources.

B. Organizational structure—the formal and informal organization of the hospital and the nursing department.

C. Characteristics of members of the organization—age, experience, education, and turnover of personnel.

D. Operating services—characteristics of the direct and indirect nursing services provided to patients.

E. Administrative services—including (1) characteristics of administrative techniques such as policies and procedures, plans, the budget, personnel programs, communication methods, and control techniques and reappraisal methods, and (2) characteristics of the administrative processes of decision-making, programming, communicating, controlling, and reappraising.

characteristics. This factor is complex and many-sided. It includes such elements as physical layout, organizational structure, characteristics of personnel, and the characteristics of the administration of nursing services. In studying the organizational characteristics of the Federal and non-federal hospitals the main purpose was to assess the extent to which each of these elements contributed to the lower nurse staffing in the Federal hospital. If some of these characteristics were found to promote the efficient use of nursing personnel in the Federal hospital which thereby enabled it to operate with fewer personnel than the non-federal hospital, some solutions to the chronic problem of the nursing shortage might be demonstrated by this study.

Data on the organizational characteristics of the hospitals studied were obtained from a variety of methods, including the use of existing records, interviews, direct observation, and questionnaires. A summary of the specific factors studied is contained in Table 2.

FINDINGS

During Fall, 1959 an intensive study was conducted in the three hospitals to determine the extent to which each of the factors outlined in Table 2 contributed to the fact that the Federal hospital was operating with 63.1 fewer nursing personnel per 100 patients than one of the non-federal hospitals and almost 80 fewer nursing personnel per 100 patients than the other non-federal hospital. A complete report of the findings of the study is contained in the author's dissertation, which also provides a detailed description and rationale of the methodology that was used.[6] These findings will be briefly summarized in this article.

The findings of this study rather clearly suggest the extent to which the factors shown in Table 2 enabled the Federal hospital to operate with considerably fewer nursing personnel than the non-federal hospitals. These findings, summarized in Table 3, indicate that about 20 per cent of the total difference in staffing could be attributable to a lighter workload in the Federal hospital; 20 per cent could be due to the fact that the Federal hospital was understaffed; and 60 per cent seems to be related to differences in organizational characteristics of the Federal and non-federal hospitals. Thus, it would appear from this study that a hospital with a smaller workforce than another could meet the same workload and attain an equivalent level of adequacy of services because of certain organizational characteristics which permit it to make more effective use of its personnel.

Among the characteristics of the Federal

TABLE 3

ESTIMATE OF THE LOWER NURSE STAFFING IN THE FEDERAL HOSPITAL ATTRIBUTABLE TO THE VARIOUS FACTORS STUDIED

	Number of nursing personnel per 100 patients	Percentage of total difference
Staffing of nonfederal hospital	113.0	
Staffing of Federal hospital	49.9	
Difference in staffing attributable to all factors	63.1	100.0
Factor		
Workload	12.6	20.0
Patients in the Federal hospital had fewer requirements for nursing services		
Adequacy of Nursing Services	13.3	21.0
Nursing personnel in Federal hospital reported greater feelings of workpressure. Thus, Federal hospital seemed to be shortstaffed		
Organizational Characteristics	37.2	59.0
Physical layout—Federal hospital used large open wards	3.3	5.2
Organizational structure—Nursing units in the Federal hospital were larger, more homogeneous, more flexibly staffed	7.5	11.9
Lower turnover of personnel in Federal hospital	10.4	16.5
Operating services—Nearly half of the Federal patients ate in dining room; no delivery room, and fewer surgical services in Federal hospital	5.0	7.9
Administrative services—Administration was more systematized and more active in the Federal hospital. Use of administrative tools was greater	11.0[a]	17.5

[a] Includes cumulative error of estimate of the effects of other factors.

hospital contributing to lower staffing were: the use of large open wards, a more simplified organizational structure with larger, more homogeneous and more flexibly staffed subdivisions, lower turnover among personnel, the use of a central dining room to feed nearly half the patients, and the more conscious utilization of adminstrative techniques and processes including an effective system of personnel policies and a comprehensive budget system which forces attention to matters of economy and efficiency. Since some of these characteristics can be applied in a non-federal hospital, the findings of this study suggest some solutions to the problem of the nursing shortage which do not necessarily entail numerical increases in personnel. As Lambertson recently remarked, a hospital's staffing ratio is "not an indication of the amount of time utilized efficiently."[7]

From these findings the question arises: How much of the lower staffing in the Federal hospital might be attributable to characteristics which could be applied in non-federal hospitals to achieve greater productivity of personnel? It would appear from the findings that not all of the difference in staffing between the Federal and non-federal hospitals was due to factors which could be replicated from one type of hospital to the next. Some characteristics were internal and unique properties of the specific hospital or the system it represented. Thus, lower personnel turnover in the Federal hospital was probably not solely a function of better personnel policies, but might also be related to the fact that fewer of its personnel were married and thus less apt to leave

because of family responsibilities. Likewise, some of the savings of personnel attributable to organizational structure might well have been achieved because of the particular characteristics of the Federal hospital's patients, its medical staff organization, and the more limited range of services it was providing. For example, it was found that it takes less nursing time if patients are grouped in large open wards as in the Federal hospital. Nevertheless, such a layout cannot easily be used by non-federal hospitals because their patients expect privacy.

The findings thus reveal that certain organizational characteristics of the Federal hospital appear to account for the fact that it could meet a workload equivalent in volume and adequacy of services to that of the non-federal hospital with 37.2 fewer personnel per 100 patients. Although not all of these characteristics are indicative of greater efficiency in the Federal hospital, a sizeable portion of the lower staffing in the Federal hospital seems to be related to characteristics that can be applied to non-federal hospitals. As such they may be considered as factors of efficiency which can contribute to a more productive utilization of nursing personnel. These characteristics of the Federal hospital include:

1. A simplified organizational structure using larger and more homogeneous bedside nursing units.
2. Use of flexible pattern of assignment of personnel to match staffing to patients' requirements.
3. Establishment of systems that relieve the nursing department of essentially non-nursing responsibilities, such as the use of a central dining room for feeding ambulatory patients.
4. Employment of personnel with sufficient experience and educational preparation to be capable of making independent decisions in their work.
5. Maintenance of an attractive personnel system to promote stability of staff.
6. Establishment of "organizational memory" through documentation of objectives, policies, procedures and accomplishments, to facilitate coordination and continuity of operations.
7. Use of structured channels of communications such as committees and conferences to exchange ideas and information.
8. Encouragement of participation in administrative processes of all members of the nursing department.
9. Participation of the nursing department in the process of budgeting which provides an instrument for systematic planning and gives insight into the financial impact of the operations of the nursing department.
10. Use of a continuous system of reappraisal to seek ways of improving utilization of personnel.

It is possible to make a conservative estimate of the fewer nursing personnel in the Federal hospital attributable to those organizational characteristics which can be called administrative efficiency. This estimate can be stated as follows: administrative efficiency may account for a little more than half of the 37.2 fewer nursing personnel per 100 patients attributable to all organizational characteristics of the Federal hospital. In other words, after equating the Federal and non-federal hospitals for workload and adequacy of services, and after discounting factors which cannot be replicated from one hospital to the next, the Federal hospital seems able to operate with 20 fewer nursing personnel per 100 patients because of what can be called greater administrative efficiency.

Conclusion

Although the hospitals studied here are too small a sample to permit broad generalizations, it is interesting to speculate what a saving of 20 personnel per 100 patients would mean to the total universe of non-federal hospitals. Since at the time of this writing there is an average daily census of 450,000 patients in all non-federal general hospitals, the ratio of 20 nursing personnel per 100 patients represents a theoretical workforce of 90,000 nursing personnel. The conclusion to be drawn is not that these personnel are unnecessary and could be elimi-

nated with improvements in administrative efficiency; rather, the conclusion is that with more effective use of the skills of nursing personnel currently employed in hospitals, productivity could be increased to help close the gap between nursing needs and supply. Thus, while it is true that hospitals are understaffed, some of the shortage probably lies in failure to make the most productive use of presently employed personnel. It is strongly suggested from this study that the nursing shortage does not consist entirely of lack of sufficient numbers of personnel, but may also be attributable to the nature of the administration of nursing service.

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DR. BURNEY JOINS TEMPLE UNIVERSITY

Dr. Leroy E. Burney, who, in January of this year, completed a four-year term as Surgeon General of the United States Public Health Service, has been appointed to the newly created position of vice president for the health sciences, Temple University, Philadelphia. This was effective as of July 1.

Dr. Burney is president of the Association of Military Surgeons of the United States this year and will preside at its 68th Annual Meeting to be held in Washington, D.C., November 6, 7, and 8. For the past six months he has been completing some work at Geneva with the World Health Organization.

In his new position, Dr. Burney will have administrative responsibility for all educational activities relating to the health sciences at Temple University: the hospital, the schools of medicine, nursing, medical technology, dentistry, pharmacy, and oral hygiene.

They Served the Sick, in North and South

By
R. MARTIN

THE Civil War had started; nurses were needed. Responding to the call at the beginning and serving to the end of that War, Daughters of Charity of St. Vincent de Paul, a Roman Catholic sisterhood, nursed the sick and wounded in both the Confederacy and the Union, regardless of color, creed or political affiliation. Thus they continued the tradition of military nursing by women, which was initiated by members of their Order in 17th century France. French Daughters of Charity had served as nurses on French battlefields from Chalons in 1653, where they were called by Queen Anne of Austria, to the Crimean War that ended in 1855.

In the United States, the Civil War gave members of the Order's American branch, established in 1809 by Venerable Elizabeth Seton, their initial opportunity for service on what was termed "the Field of Action." Eyed distrustfully by many persons at the start, their gull-winged white bonnets known as cornettes became acceptable as flags of truce.

First Manassas (Bull Run) fought on July 21, 1861, the first major encounter of the war, found the women of this sister-

FIG. 1. An original sketch by an anonymous artist of the day shows Union prisoners from Massachusetts, captured in the First Battle of Manassas (Bull Run), being served by a Daughter of Charity at the General Hospital in Richmond, July-August, 1861. The note accompanying this sketch read: "Dorchester Boys, All. At the window, General and Mrs. Ricketts." (Civil War records now at the National Archives, Washington, state that Captain—later, General—Ricketts commanded the First U. S. Artillery at First Manassas, where he was wounded, taken prisoner and later exchanged.

TABLE 1

CIVIL WAR LOCATIONS WHERE DAUGHTERS OF CHARITY SERVED

Place	Date	Accommodations	Pats.
Mobile, Alabama	1862	City Hospital* Marine Hospital	Confed. Confed.
Montgomery, Ala.	1861	?	Both
Washington, D. C.	1861–65	Providence H.* Eckington H. Cliffburn H. Lincoln H.	Union Union Union Union
Warrington, Florida	1861	Improvised	Confed.
Atlanta, Georgia	1863	Tents	Confed.
Marietta, Ga.	1863	Hospital	Confed.
Alton, Illinois	1862–65	Milit. Prison	Both
Camp Moore, Louisiana	1861	Camp Hosp.	Confed.
Monroe, La.	1862–63	Camp Hosp.	Confed.
New Orleans, La.	1861–62	Charity Hosp.* Hotel-Dieu* Marine	Confed. Union Confed.
Antietam, Maryland	1862	Fields, improv.	Both
Boonsboro, Md.	1862	Fields, improv.	Both
Frederick, Md.	1862–64	Revolutionary War Barracks	Both
Point Lookout, Md.	1862–64	Tents, etc.	Both
Sharpsburg, Md.	1862	Improvised	Both
Holly Springs, Mississippi	1861–62	Temporary Hosp.	Confed.
Natchez, Miss.	1862–63	?	Confed.
St. Louis, Missouri	1862	2 Fed. Milit. Pris.	Both
Gettysburg, Pennsylvania	1863	Many improv.	Both
Philadelphia, Pa.	1862–65	St. Joseph's Hosp.* Satterlee Hosp.	Both
Danville, Virginia	1862	Improvised	Confed.
Gordonsville, Va.	1862–	Milit. Hosp.	Confed.
Lynchburg, Va.	1862–65	Hosp., Factory	Confed.
Manassas, Va.	1862	Improvised	Both

TABLE 1—*Continued*

Place	Date	Accommodations	Pats.
Norfolk, Va.	1861	St. Vincent's Hosp.*	Confed.
Portsmouth, Va.	1861	Marine Hosp.	Union
Richmond, Va.	1861–65	St. F. de Sales Inf.* General Hosp. Others	Confed. Both Confed.
White House, Va.	1862	Improv., transports	Union
Winchester, Va.	1861	Hospital	Confed.
Harpers Ferry, West Va.	1861	Hospital	Confed.

* Already operated by the Sisters of Charity.

hood ready to care for battlefield casualties arriving in the capitals of both Confederacy and Union. A brief account of their activities at the general hospital in Richmond in July, 1861, was written by one who served there, Sister Rose Noyland.

With seven other Daughters of Charity, Sister Rose went from St. Joseph's Orphan Asylum in Richmond on July 26 to nurse at the General Hospital, also known as the City Hospital. A new building designed as the City Almshouse, it had been taken over for military purposes.

Here is her own story, appearing for the first time in print:

"We found three hundred sick and wounded Confederate and Federal soldiers. Many of those poor soldiers lay on the battlefield several days un-

June 1861 & July 1861 — 1

		Admission	Dis.	Age	Nativity	Occupation
1	Lawrence O'Toole	June 27th	July 2nd	25	Ireland	Engraver
2	Jane Hopkins	July 2nd	" 8th	18	Washington	
3	Barbara Rhoad	" 4th	" 10th	21	Germany	Domestic
4	John Shanahan	" 10th	Sept. 21st	11	Washington	
5	Leopold Charriet	" 15th	Aug. 5th	25	France	25th N.Y. Vol.
6	Edward Cunningham	" 19th	" 10th	22	Ireland	Laborer
7	John B. Stuart	" 21st	" 4th	35	S. Carolina	Lieut. U.S.N.
8	Joseph Clemency	" 22nd	" 6th	20	Washington	Laborer
9	William Behan	" "	" 2nd	20	N. York	71st N.Y. Vol.
10	George A. Cooke	" "	" "	19	"	"
11	Elizabeth Roney	" 30th	" 3rd	18	Washington	Domestic

FIG. 2. First page of original register of Providence Hospital, Washington, D.C., for June-July, 1861, shows that several of the first wounded from Manassas (First Bull Run) were received there.

FIG. 3. Providence Hospital, Washington, D.C. as it appears today. Originally located on Capitol Hill area, now in northeast part of city, at 1150 Varnum Street, N.E.

der sun and rain. Their wounds were gangrenous. We spent days scraping maggots and cutting away rotten flesh. In a few days we got good food and clothing for them.

"Sunday night, eleven prisoners were brought to the hospital. Sisters Philip and Rose were told to stay up to receive them. They didn't know where they were being taken to, but when they saw the cornettes, prisoners as they were, they gave three cheers for the Sisters of Charity at twelve o'clock at night!

"We gave them a good supper of coffee, bread, butter and ham. They said it was the only good meal they had had since they left their homes. We gave them clean rooms and beds.

"Among them were Majors, Colonels, Captains, and Lieutenants. Sister Blanche procured them some musical instruments. Playing and singing helped to while away the time. After some weeks, the officers were sent to the Libby Prison and from there exchanged.

"Mrs. President Davis (wife of Jefferson Davis, President of the Confederacy) often came to the hospital to see the sick Union soldiers. She supplied them with tobacco, cigars, soap, razors, and anything they asked for. She requested the Sisters not to let patients know who she was. The Confederates, she said, she knew would want nothing. The soldiers were most grateful and respectful to the Sisters.

"A Protestant minister who was a constant visitor at the hospital asked me if I was ever tired. I told him I was, very often. 'You must get a large salary for what you do?' I told him no less than the Kingdom of Heaven."

Some of the first battlefield casualties from Manassas were cared for by other Daughters of Charity at Providence Hospital in the capital of the Union, about 25 miles removed from the fighting. According to the original Register of this hospital, two privates of the 71st New York Volunteers, William Behan, 20 and George A. Cooke, 19, were admitted July 22, 1861, the former listed as suffering from "wound of thigh." Both had been wounded at First Manassas the day before. First Confederate prisoner to be received at Providence, on July 30, was J. A. Wingfield of the 19th Virginia Volunteers, described as suffering from "general debility."

Throughout the war, Providence was the sole privately-operated hospital in Washington, and the only hospital there to admit civilians as well as soldiers and sailors. Of some 85 war-time hospitals opened from 1861 through 1866 in the District of Columbia and Alexandria, it is the only one that has remained continuously open until today. Founded June 10, 1861 by four young Daughters of Charity from Emmitsburg, Md., Providence Hospital is now commemorating its Centennial Year, which coincides with that of the Civil War.

Of a total of some 571 members of twelve Roman Catholic Sisterhoods who nursed the sick and wounded in the Civil War, at least 250 were Daughters of Charity. They served without compensation in military hospitals, prisons, hospital ships, and improvised aid stations on or near the battlefields. Responding to requests from the Surgeons General of both Union and Confederacy, they went "wherever suffering humanity could be found" and cared impartially for all. Their ability to carry out instructions, to administer medicines and prepare meals on schedule, and to maintain cleanliness, order and quiet in the wards was appreciated by the overworked Army surgeons on both sides.

Providence Hospital
1150 Varnum St., N.E.
Washington, D.C.

Effect of the American Revolution on American Medicine

By
HOWARD LEWIS APPLEGATE

IV

HISTORIANS of American science emphasize the fact that medicine in America radically changed during the Revolutionary period, 1775-1783. It is quite true that the war profoundly affected medical science, both negatively and positively. Wartime emergencies stimulated great progress in certain branches of the medical arts, while in other fields, the mere presence of strife and absence of normalcy provided unfortunate setbacks.

The outbreak of hostilities in 1775 naturally altered the conditions under which medical science had been encouraged in the colonies. The institutions, men, and the interrelationships which had supported colonial medicine were badly disrupted by the war. Contacts with British scientists and medical schools were no longer possible. Furthermore, at one time or another, the British occupied most colonial cities, the centers of intellectual and medical activity. Meetings of the provincial medical societies were generally discontinued and the professional school at New York was closed and the one at Philadelphia suffered a decline in student attendance. The normal flow of correspondence, books, journals, and freshly graduated students from Great Britain was severely reduced. It should also be noted that some of the best educated and most successful colonial doctors remained loyal to the crown.[1]

As a result of wartime experiences, great value was attached to professional medical education. Whitfield Bell has estimated that of the 3,500 colonial physicians in 1775, only about 400 had medical degrees or university training. This small minority and a few hundred other competent men, who were self-taught or graduates of the apprenticeship system, did achieve some distinction and reputation. Prior to 1775, the majority of young men seeking to become doctors had to be content with training as apprentices to local practitioners, who took them into their offices, let them read books, taught them to prepare medicines and compound drugs, and gave them first hand observation of treatment. Yet, the men who were given positions of responsibility in the Continental hospital were all university trained men. In fact, Directors General John Morgan and William Shippen had organized the medical department of Philadelphia college in 1765 and John Jones, a district medical director, founded the Kings College Medical School in 1768.[2] It soon became apparent that college trained men passed the medical corps qualifying examinations more readily and obtained promotions more frequently than did those men who were self-taught or had little training. When the war ceased, a premium was placed on professional medical education. Consequently, attendance of the schools at New York and Philadelphia increased, and several other colleges created medical faculties.

The war gave impetus to the examining and licensing of physicians by state authorities. The Continental Congress and several states created Examining Committees which tested all applicants for military medical posts in the subjects of anatomy, physiology, surgery, and physic. State leaders reasoned that if it was necessary to examine and license military surgeons, then it was equally essential to protect civilians from incompetent doctors or quacks. Therefore, several northern states required all civilian practitioners to be tested and commissioned. Shortly after the conclusion of the war, most other northern and middle-Atlantic states followed suit.[3]

Doctors from various sections of Amer-

ica had unusual methods and techniques which had resulted in provincialism in medical thinking and practice. Army surgeons, who previously had lived in isolated areas, now came into contact with other military medical officers, with whom they discussed medical treatment and exchanged ideas, formulas, and remedies. In these ways, medical provincialism was broken down and eventually replaced by newer and more progressive thinking. American physicians also observed the work of British, Hessian, and French doctors. James Thacher, who had worked with the British and Hessians at Saratoga noted that, "The English surgeons perform with skill and dexterity, but the Germans, with few exceptions, do no credit to their profession; some of them are the most uncouth and clumsy operators that I ever witnessed."[4] The French medical officers were more influential because their medical tradition was unknown in America, because they were superior hospital administrators, and because their hospitals were easily accessible to American doctors. Jean Francois Costé, the French army chief physician, spoke before medical society meetings, published a brief pharmacopoeia for use in military hospitals, and wrote an account of his experiments treating venereal disease with opium.[5]

The Revolutionary War gave medical men greater opportunity for investigation, particularly in surgery. At the outset of the conflict, few colonials were skilled surgeons, and most of these men were unaware of the complicated operations in military hospitals. After much initial study and practice, many military doctors became skilled surgeons. Experimentation on the dead and dying added much information to medical knowledge. Despite civilian objections to human dissection, some army surgeons experimented on the bodies of dead soldiers, which had never been claimed by relatives or friends. Other physicians worked in the field of remedical medicine. These investigators lectured on their research to their fellow surgeons.[6]

The needs of the Continental Hospital stimulated the domestic manufacture of instruments and processing of drugs. Most of these items had been previously imported, but the war cut America off from her British and Imperial sources, and as a result, Americans had to make many of their own instruments and drugs. Congress gave bounties to instrument makers, whose first efforts were crude reproductions of older European models. As the war progressed, newer and better instruments were made. There is little difficulty in processing drugs if the basic raw materials are available. Since few basic ingredients were produced in America, some apothecaries developed substitutes, which did not have the medicinal value of the original drugs, but at least partially alleviated pain and infection. For example, one Joshua Clayton compounded a powder made of poplar, dogwood, and white oak bark and roots, which was substituted for the scarce Peruvian bark.[7]

A number of significant medical treatises were published as the result of wartime experiences. In 1775, John Jones printed his *Plain Concise Practical Remarks on the Treatment of Wounds and Fractures.* This book, though not original, was the first compendium of European military medical manuals to be published in America. John Morgan's pamphlet on smallpox, *Recommendation of Inoculation according to Baron Dimsdale's Methods,* was published in 1776. William Brown, an army physician general, spent his spare moments writing a *Pharmacopoeia for Use of Army Hospitals* (1776), a Latin work which was the first book of its kind written in America. Perhaps the most important work written as a direct result of the war was Benjamin Rush's *Directions for Preserving the Health of the Soldier,* published by Congressional order in 1778. In his *Regulation for the Order and Discipline of the Troops of the United States,* issued in 1779 by the Board of War, Baron von Steuben offered sound advice on the care of sick and wounded and on hospital administration. James Tilton's *Economical Observations on Military Hos-*

pitals and the Prevention of Disease Incident to an Army (1813) contained practical comments on hospital architecture, medical administration, causes of diseases common to armies, and care of the sick and wounded.

Many other pamphlets were based on wartime research and investigations. Dr. Ebenezer Beardsley wrote an account of the cause, spread, and treatment of dysentery in a Continental regiment. Dr. Barnabas Binney described the healing of a particular kind of gunshot wound. Hugh Martin published a pamphlet which narrated experiments through which he hoped to develop a cure for cancer. Benjamin Rush's booklets on military diseases, tetanus, smallpox, and alcoholism were all partially based on his army experiences.[8]

Military surgeons made some progress in preventive medicine. They discovered that ailments common to the armies could be decreased by control of certain fundamental factors: physical condition of the soldiers, shelter, clothing, exercise, weather, use of food, water and alcoholic beverages, and rules of personal cleanliness and camp sanitation. The threat of smallpox was greatly reduced when inoculation was adopted and perfected after several years of trial and error.

Many historians and most Americans consider the Revolution of 1775 as a blessing because it severed the colonies from the tyrannical yoke of older world imperial control. The blessings of a free and united America were to come in the long range future, because immediately after the Revolution, the new nation had a difficult road ahead of it. The story of American medicine parallels our national development. The war began to break the old world dominance of medical science, and the older armies of superstition and ignorance began to suffer their first setbacks. As in the growth of the country, the progress of medicine was slow, but the Revolutionary War stimulated: emphasis on professional education and licensing of doctors, use of progressive medical practices, experimentation, creation of domestic instrument and drug industries, spread of medical information in books and periodicals, and growth of research in preventive medicine.

(To be continued)

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EDITORIALS

Animal Experimentation

MILLIONS of dollars are spent yearly by the Federal government, by corporations, and by Foundations for research in the many perplexing problems in yet unconquered diseases. This research requires the use of animals at some point along the way. Without the use of animals the research would be fruitless.

Unfortunately there are some persons in this enlightened country of ours who would deprive the researchers of the very tool they need, the animal. This group shouts its opposition so they are heard, and too frequently by persons of political leanings rather than medical training. Such persons are ready to accept the benefits of all the medical research but raise objection to one of the important methods—the use of animals. Next thing we know they will be wanting to get to the moon by thinking they are there, but not by travelling on a space ship.

Animal experimentation is vital to the medical researcher. Of course, no one but a sadist would want to treat an animal cruelly. In the "Principles of Laboratory Animal Care" which have been developed by the National Society for Medical Research we have the rules laid down for the humane treatment of these animals.

Now from time to time bills are introduced in Congress which if enacted and enforced would seriously curtail medical research. These bills pertain to the use of animals in the laboratory. Is this not an inconsistent action when our Congress is appropriating more and more money, many millions as a matter of fact, for medical research?

We are either for or against medical research. If we are for it then we must be for animal experimentation; that is, we must be for the use of animals in the research. It cannot be any other way.

Blood

THERE is a growing concern among some in the medical profession about the number of blood transfusions that are being given. More and more articles are getting into the medical literature.

"Transfusions by the Gill," an article by Dr. Robert S. Myers, Executive Assistant Director of the American College of Surgeons (Bull. A.C.S., Vol. 46, No. 2, 1961), points out the abuse of blood transfusions; examples of which are those "prescribed as a tonic," and the "routine use in surgery."

In his article Dr. Myers refers to Dr. W. H. Crosby's statement ("Misuse of Blood Transfusion," Blood, 13: 1198-1200, 1958), that seven grams of hemoglobin per 100 milliliters are sufficient for tissue oxygenation for most situations during surgery and that 10 grams at the start of surgery provides adequate leeway.

If a person with a normal blood volume can give a pint of blood, is it not reasonable to assume that the loss of that amount of blood does not call for a transfusion?

Maybe blood transfusions have been overdone. This is the time for re-evaluation. We need clear thinking on this problem for guidance in our disaster situations. There are so many things to be done at those times that complicating matters by giving even one unnecessary blood transfusion should arouse our attention.

We must look to those who can speak with authority on the subject, then follow their guidance. The blood transfusion for therapeutic reasons seems to need some revision.

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Around the World

(Ser. IV, No. 7)

By

CLAUDIUS F. MAYER, M.D.

GERMANY knows how to exploit its natural resources for the health of its citizens. At the Salzeemen station and at the Dermatological Clinic of the Magdeburg Medical Academy, patients are given a special kind of treatment in a grotto 400 meters underground. This grotto is in the *salt mines of Schönebeck,* near Magdeburg. Patients are carried to this place three times a week. They sleep there for three nights. Experience showed that in the underground galleries of the mine the air is completely sterilized, there are no pollens of flowers, the atmospheric pressure is higher, and the temperature is constant. This is very favorable for the treatment of bronchial asthma and even for certain skin diseases. According to the reports, the underground clinic leads to excellent results.

In France, the organization of *centers of respiratory reanimation* was found to be essential. Actually, several such centers are going to be opened in the near future. They will function in the larger hospitals. The work of the reanimation center attached to the Bichat Hospital was recently described to the French Academy of Medicine. During ten months this center received 117 patients of whom 14% died within the first day of admission. The reanimation center at the Bichat Hospital has only 7 beds, but the center at the Claude Bernard Hospital has about fifty beds. Patients who need the services of such institutions either had an emergency tracheotomy, or were comatose from poisoning with barbiturates, with carbon monoxide, or they suffered from severe type of asthma, emphysema, sclerosis of the lungs, etc. Neurological respiratory difficulties from poliomyelitis, from Guillain-Barré syndrome, or from tetanus, form another category. According to the organization plan, 6 to 8 larger, 50-bed centers will suffice for the chronic cases of respiratory difficulties, while the smaller reanimation centers should be more numerous, perhaps one center for every 250,000 inhabitants. Again, the main problem of the organization is not the equipment or the buildings, but the recruiting of adequate and well-trained personnel.

Based upon the concept of Selye's stress, and its various effects upon the organism, a member of the French Medical Academy now suggests that irritation of the erectile zone of the nose (i.e., the middle and lower turbinates, the nasal septum and the nasal vestibule) will result in the cure of various pathological conditions. He calls the douching of these nerve-rich portions of the nose by the term of *rhino-stress.* It can be repeated at 3-day intervals, or longer. It brings beneficial effect in headaches, facial neuralgias, sciatica, all sorts of allergic manifestations (migraine, asthma, vasomotor rhinitis), paroxysmal tachycardia, angina pectoris, flatulence, dyspepsia, acute cholecystitis, many syndromes of the imbalance of the vegetative nervous system. Eight to ten rhino-stressing douches are usually required to complete a cure.

The so-called *Diego blood factor* was discovered in 1953 at Caracas, Venezuela, by Larysse on occasion of a fetal-maternal isoimmunization in a mestizo family. Since then, numerous investigations were made on this blood-group system, and it was found that it is present only in certain racial groups. For instance, the Diego factor was never found in a white man or in a pure Negro. On the other hand, it is rather frequent in Mongoloid people, thus in the American Indians (with the exception of the Eskimos), in mestizos, and in such Asian races as the Japanese, Chinese, while it is again completely absent in the Australian aborgines, and in the Polynesian

tribes. Bio-anthropologists draw from this the conclusion that the American continent was originally populated by Mongoloid tribes who migrated there from a cradle situated in the center of Asia, via Alaska, and pushing their way forward down to South America.

The International Committee of the Red Cross recently published a new edition of a booklet which contains the *Geneva Conventions in pictures*. The illustrations are from the 1949 conventions. Each picture is accompanied by a short commentary in nine languages, French, English, Chinese, Russian, Japanese, Arabic, Spanish, German, and Hindi. The first edition of the booklet was issued in 1957. A special edition was also prepared for the use of the Congolese in which the Hindi text was substituted by Lingala, the most widely spoken dialect in Leopoldville Province, and in the Congo Armed Forces.

This year, and last month (June 1961), the Municipal Council of San Remo, Italy, inaugurates an international *cardiology prize "City of San Remo"* to encourage and to recognize the progress which medical science has reached in the study of the physiology and pathology of the heart. San Remo is a climatotherapeutic resort where cardiac patients used to get their rest and required treatment. The value of the prize is ten million liras, and the award will be presented on 23 June, the date of the first centenary of Italian unity, at the Torino meeting of the Italian Cardiological Society.

The prize may go to a foreigner or to an Italian scholar. Italians themselves are very active in biological and medical research as we can see, for instance, also from the numerous grants given this year by the *Italian National Research Council* to the various medical institutions. Thus, the staff of the Eye Clinic of Modena University was helped by the Council to obtain proper equipment for the study of the intraocular circulation of blood. At the Clinic of General Medicine of Rome University, experimental and clinical researches are carried out on the principles and application of spatial vector cardiography. Arteriosclerosis is studied at the Modena Medical Clinic. The Palermo Anthropological Institute received a grant for the anthropometric survey of the Sicilian population, while the Hygiene and Microbiological Institute of Palermo University is being supported in the study of the biology of Treponema pallidum. The Padova Zoological Institute is helped in its researches on gametogenesis and reproduction, while the Firenze Microbiological Institute received two million liras for studies of inhibition of the influenza virus. The Torino Pathological Institute is engaged in the study of the metabolism of tumor cells by means of radioactive isotopes. The Forensic Medical Institute of Palermo conducts experiments on head injuries, and the Obstetrical Clinic of the Torino University devotes time for the investigation of the pathological anatomy of uterine cancer.

The world-wide experience with the orally administered attenuated live poliovirus is favorable. The *vaccination with live poliovirus* was often carried out during poliomyelitis epidemics, and it has given a very high percentage of immunity. Thus, at the 1958 epidemic in Antiochia, Colombia, not a single case of polio developed in the vaccinated persons, or in those who came in contact with them. In the same year, at Singapore, where the epidemic was caused by Type I virus, out of almost 200,000 vaccinated children only 6 developed a paralysis, while thirty times as many had paralysis among the non-vaccinated children. Similar results were seen in the Congo, in Nicaragua, in the U.S.S.R.(Tashkent, Estonia, Lettonia), etc. A huge field trial was made in 1959 in Czechoslovakia. In this country, both the Sabin live vaccine and the Salk dead vaccine were used at different areas of the country. It was observed that the polio epidemic recurred at a higher frequency in the Salk-vaccine immunized areas, while no increase in the polio rate was seen in the Sabin-vaccine immunized areas of the country. The question of Sabin vs. Salk vaccine is not completely solved, however. Yet, the Sabin vaccine is definitely gaining ground in all countries outside the U.S.A. The French ex-

pert, Lépine, cautiously suggested that perhaps the Salk or attenuated dead vaccine could be used as a first approach of immunization to protect against the rare possibility of a neurological complication which might come from the use of the live vaccine of Sabin.

In Australian New Guinea a new hospital was built. The Madang hospital opened recently. It is a major permanent district hospital to provide full range general medical and surgical facilities for *Papua-New Guinea.* The Territory now has 105 administration hospitals which last year treated a total of 100,000 patients. The new hospital will also train nurses.

The University College Hospital at Ibadan, *Nigeria,* has a Students' Clinical Society. This society has established a new journal called *"Dokita,"* a title which is the Nigerian nickname of "doctor." The journal will be issued quarterly, and it contains also articles interesting for geopathology and geomedicine, and for the folk medicine of the country (e.g., an article describes the practice of quack doctors in a Yoruba village).

The whole world of medicine will remember Jules BORDET (1870-1961), 1919 Nobel laureate, who died April 6 at the age of 90 at Bruxelles. He was the founder and director of the Pasteur Institute at Bruxelles, and the most eminent among the present-day bacteriologists and immunologists. His name and that of Gengou are associated with the discovery of Hemophilus pertussis, and with the complement-fixation reaction. His work on this reaction appeared in 1901, and formed the basis for the Wassermann reaction for syphilis, and for many other diagnostic tests.

The *Swedish Dental Association* celebrated its *100-year anniversary* last August, with the arrangement of an international Centennial Congress at Stockholm. About 1,600 dentists participated from 28 countries. The main topics of the scientific lectures were (a) the prevention of caries, (b) prevention of paradentosis, and (c) prevention of developmental abnormalities of the facial bones and the jaw bones. Among the individual lectures, one was by an American (Armstrong, of Minneapolis) who discussed the metabolism of fluorine in the denture.

Near Moskva, the Russians started the *construction of a new oncological experimental institute,* and clinic of the U.S.S.R. Medical Academy. It will be the largest of such centers not only in Russia but in the whole world. It is built on a 16 *ha* area, and it will have 30 different buildings, a city of health in itself. The entire scientific activity will be concentrated in 7 main buildings, the largest of which will have 5 stories for all the required laboratories of cancer research. There will be also a conference room for 700 persons, with television screen. The clinical section will have two buildings, one with 360 beds, the other with 30 beds. In the latter, the treatment with radioactive substances will be carried out. The most modern types of communication will be available. Visitors can get into conversation with the patients by vidiphone (telephone with a video screen). By the way, the International Congress of Oncology will be held in Moskva in 1962.

Reports from Red China are more and more numerous on the "epidemics" which ravage the country. It is surprising that, while this term has never been used before in the Chinese newspapers, it now appears constantly in the Chinese Press. At the same time, the Chinese dailies publish all sorts of nonsense regarding *miraculous cures* which may result if people follow rigidly "the thoughts of Mao Tse Tung." One paper said that schistosomosis, a major and widespread disease in China, is now being cured in three days' time, and it was also so reported to the People's Congress in 1960. Another newspaper story mentions how a Mukden medical student invented a treatment for sea-sickness. The Party secretary who works at the Chinese Medical Academy wrote last August that, due to communist thought, now such old diseases as hypertension, ulcer, diabetes, can be cured in 2-3 weeks' time.

Li Teh-Ch'uan, Chinese minister of Public Health, a woman, made her reports on the state of public health to the Chinese Congress and the Chinese people in March and in November 1960. In her speech and in her article she claimed that in 1959, a total of 70 million Chinese were under treatment for schistosomosis, filariasis, tape-worm and malaria, and the greater part of these people were cured. No other statistics are quoted; indeed, statistics concerning the data on epidemics are kept in the secret archives. It may be assumed that today the number of western-educated physicians may be around 60,000, or 1 doctor to about 10,000 Chinese.

Much is said nowadays about *village hospitals in Red China.* But, these are indeed not hospitals in the western sense. Such a hospital was set up for instance in *Inner Mongolia* at Salachi, a town with a population of 50,000. The hospital has 20 beds, and a staff of 87. But what a staff! The Communist Party's executive committee decided that 32 medical personnel of low technical standard should study medicine and surgery, without interrupting their own daily work. After 5 months, they undertook major operations, on the stomach, on the intestines and the uterus. They improvised their own medical instruments. This was published with the remark that "This proves that under the guidance of the Party, if the masses are mobilized, all obstacles are broken down and all difficulties overcome" (quoted from the 9 May, 1960 issue of the Huhenot Daily, published in Inner Mongolia).

About the size of the epidemics, news of which the Chinese official reports wish to suppress, we may judge by the huge emergency measures that the officials had to take. Thus, last July, an unnamed contagious epidemic in Szechuan province required the mobilization of 110,000 persons for public health in the villages. In August, such an unnamed health hazard required the wholesale examination of the entire population (ca. 3,000,000) of Tientsin City. Everywhere trouble developed, mostly from the village dining-halls. Widespread poisonings were reported.

The major predisposing factors of the Chinese epidemics are subnormal nutrition, lack of vitamins, of protein, of carbohydrates, unhygienic food-handling, and intestinal parasites from human feces. The use of human feces is encouraged as fertilizer. Although a conference was held in 1959 on how to *sterilize human feces by heat,* the farmers are unwilling to heat the feces in big pots as demonstrated. The Chinese peasants are shocked by saying: "The pots are for cooking rice, and you people are cooking feces."

Recently, more and more physicians are sent from the cities to the rural areas. To do what? To work as peasants, or to correct the bad living and producing habits of the Chinese agricultural population? The doctors were deeply shocked, apparently by seeing such misery in the country in the form of malnutrition and epidemics. The doctors also witness the relentless drive of the communist agitators. They themselves are under pressure by the Party secretaries who want the patients back to work as quickly as possible. The doctors try to resist while they are accused that they do not wish to adjust their methods to the new times. The old herb medicine and the western medicine are also in constant struggle, adhering to their independence in spite of all the pressure from the communist leaders. The side-by-side existence of the *"canonic Recipe School"* (Ching Fang P'ai) and of the so-called *"Modern School"* (Shih Fang P'ai)—which in fact started during the Sung dynasty about 1000 years age—also show that something strong is in old China which no new political power of Red China can break!

In the March issues of the Chinese journals it was reported that now many medical and health units of the Chinese People's *Liberation Army have dispatched medical teams* to the rural areas to assist the rural communes in the control work of the "expanding spring disease." These military

medical units are sent by the Chief Logistics Directorate to such places as Shantung and environment, the Shenyan area, Wuhan, Nanking, Canton, Tsinan, Chengtu, Fukien. The Chinese Navy, Air Force and other branches of the Armed Forces also ordered a number of medical personnel to serve in the rural areas. These units have much to do, including even nursing of the sick. They also "train" new doctors, nurses and health officers by the apprenticeship system. The report says that one of such military medical teams trained "200 doctors, health officers and midwives" in a month. Indeed, we may wonder what all these reports really mean.

Early this year (1961) the *New Zealand Medical Society* held its annual meeting at Auckland. The sessions of the Psychiatry Section were particularly interesting. A Wellington psychiatrist commented on *humor as an element of mental health.* The study of an individual's sense of humor usually yields clues to his personality structure and psychopathology; it also indicates his personal, cultural and social attitudes. Recovery from mental illness can be sometimes traced to the re-emergence of a sense of humor. The psychiatrists should also have a sense of humor, and as a mature specialty, psychiatry should be capable of laughing at itself. (This may be questioned by others.)

A group of the New Zealand psychiatrists talked about the *increased addiction to alcoholism* all over the world. In New Zealand, the estimate states that there were between 15,000 and 20,000 chronic alcoholics. Neurotic subjects, the physically deformed, psychopaths, and sometimes the psychotic provide a fruitful soil for the development of alcoholism. For a successful treatment the willing cooperation of the patient is essential. Complete avoidance of alcohol is necessary, and the patient should be initially hospitalized. In New Zealand, among the many other facilities, there is also an *"inebriates' island"* to which alcoholics could go voluntarily, or following committal by a court.

Another aspect of the Psychiatric Section of the New Zealand Medical Association dealt with the *New Zealand black magic,* or Makutu, as practiced by the Maori. According to the Maori primitive belief, the human evil is organized by Whiro, who is represented in this world by the lizard. If the lizard is introduced into a man's body, he becomes sick or he dies. There are many "Thou shalt nots," or tabus, the breach of which means withdrawal of divine protection and exposure to the evil principles. Makutu is the calling of the evil principle for help. It can be done by the recital of spells, as practiced by the witch doctors. The Maori is apt to relate illness and misfortune to Makutu. Epilepsy is ascribed to breach of tabu. Epileptic patients and their families are therefore very resistant to any rational therapy. Moreover, the patient's *resignation to inevitability* will rob him of the powerful vital force which tends to recovery. Thus, one sick girl predicted her own death, and when it took place, no organic reason could be found for it. The belief in witchcraft and in Makutu is so strong that neither the Christian religion nor a higher education is able to break it. A Maori who had studied advanced psychology, and anthropology, still attributed his own anginal pain to Makutu. It seems to the observers that the modern renaissance of the old Maori mythology in New Zealand is a subconscious cultural reaction against the white man, a sort of collective racial rationalization of guilt, fear, superstition, and ignorance with a sentimental desire to cling to the past. . . . Multa paucis!

NOTES

Timely items of general interest are accepted for these columns. Deadline is 1st of month preceding month of issue.

Department of Defense

Senior Medical Advisor—FRANK B. BERRY, M.D.

Deputy Ass't Sec'y of Defense (Health and Medical), Off. Ass't Sec'y of Defense for Manpower—EDW. H. CUSHING, M.D.

VISIT EGYPT AND FRANCE

Dr. Frank B. Berry, Senior Medical Advisor to the Assistant Secretary of Defense (Manpower); Lt. General Leonard D. Heaton, Surgeon General of the Army; Rear Admiral E. C. Kenney, Surgeon General of the Navy; Rear Admiral C. B. Galloway, MC, USN; Colonel L. A. Potter, MC, USA; Commander H. L. Walter, MC, USN; and Commander H. E. Sinclair, MSC, USN, recently spent some time in Egypt visiting the National Research Center and Nutrition Laboratory, and MAMRU 3 in Cairo. They then flew to Paris where they were joined by Major General O. K. Niess, Surgeon General of the Air Force, for the NATO-SHAPE Conference.

DELIVERS TRIMBLE LECTURE

Dr. Frank B. Berry recently delivered the I. Ridgeway Trimble Lecture at the 163rd Annual Meeting of the Medical and Chirurgical Faculty, Baltimore.

CASE NO. 1,000,000

The Armed Forces Institute of Pathology, Washington, recently received its one millionth accession when a biopsy specimen of a tumor removed from the eyelid of a patient was received by the Institute's Registry of Eye Pathology.

Founded as the Army Medical Museum during the Civil War (May 21, 1862), the Institute has grown to become the central laboratory of pathology for the Armed Forces, Veterans Administration, FBI, Civil Aeronautics Board and Federal Aviation Agency, Atomic Energy Commission, and other governmental agencies. Today the Institute receives about 70,000 autopsy and surgical cases annually from these combined sources.

The Director of the Institute is Colonel Frank M. Townsend, USAF, MC.

LEPROSY RESEARCH

Recently at the Johns Hopkins School of Hygiene, Dr. Chapman H. Binford, Chief, Leprosy Branch of the Armed Forces Institute of Pathology, presented a lecture on "The Problem of Animal Transmission; Summary of a 5 Year Study."

He stated that the study has resulted in the isolation in several experiments of a mycobacterium which causes a granulomatous disease in the hamster. It was also found out that in the hamster, bacterium grows best in the cooler parts of the body, but grows slowly on artificial media. The mycobacterium has been transmitted, hamster to hamster, 8 times without any apparent change in the virulence or rate of growth.

Army

Surgeon General—LT. GEN. LEONARD D. HEATON

Deputy Surg. Gen.—MAJ. GEN. THOMAS J. HARTFORD

PERSONNEL MANAGEMENT COURSE

Lt. General Leonard D. Heaton opened the Personnel Management Course held at

Walter Reed Army Medical Center, Washington, June 5-9, for approximately 50 Medical Service Corps officers. The purpose and objectives of the course were discussed by Brig. General Howard W. Doan, MC, Director of Personnel and Training, Office of the Surgeon General. The course was under the direction of Lt. Colonel Oliver H. Steed, MSC, Surgeon General's staff.

WALTER REED PORTRAIT

An oil portrait of Major Walter Reed, the doctor of yellow fever fame, was recently presented to the Walter Reed Army Medical Center by the John Hancock Mutual Life Insurance Company. Presentation of this portrait by Artist Robert Riggs was made by Dr. Frank A. Warner of the insurance company. The portrait was accepted for the Center by Major General Clinton S. Lyter, the Commanding General.

Present at the presentation was 86-year-old Gustaf E. Lambert who was a hospital orderly during the yellow fever investigations in Cuba. His job was to handle the soiled linen.

The Secretary of War, Hon. Elihu Root, in his annual report, 1902, said with reference to the conquest of yellow fever in Cuba in 1900-1901:

"The brilliant character of this scientific achievement, its inestimable value to mankind, the saving of thousands of lives, and the deliverance of the Atlantic seacoast from constant apprehension, demand special recognition from the Government of the United States."

FIRST ARMY SURGEON

Colonel Knox Dunlap, MC, formerly Commanding Officer of Walson Army Hospital, Fort Dix, New Jersey, was recently appointed First U. S. Army Surgeon, Governors Island, New York.

Colonel Dunlap, a native of Ponca City, Oklahoma, received his medical degree from the University of Kansas in 1932, interned at the university hospital and served a residency in orthopedics at Brooke General Hospital, Fort Sam Houston, Texas. During World War II he was Commanding Officer of the 97th General Hospital overseas. During the Korean Conflict he was Commanding Officer of the 121st Evacuation Hospital in Seoul, and later Surgeon of the Eighth U. S. Army.

TO BAMC

Brig. General Clarence P. Canby, DC, who has been Director of Dental Activities, Walter Reed Army Medical Center, has been transferred to Brooke Army Medical Center, Fort Sam Houston, Texas.

ASSIGNMENT IN SGO

Lt. Colonel Oliver H. Steed, MSC, has been assigned to the Directorate of Personnel and Training, Office of the Surgeon General of the Army. He has just returned from Germany where he was Commanding Officer of the 8th Evacuation Hospital.

Major Harrold E. Graham, MSC, has been assigned to the Directorate of Plans, Supply and Operations, Office of the Surgeon General of the Army. He will be Chief, Distribution Section, Supply Division.

TO IRAN

Colonel Charles P. Ward, MC, has been appointed Medical Advisor to the United States Military Mission with Iranian Army. Upon his termination of duty as Commanding Officer of the U. S. Army Dispensary at Chicago, Colonel Ward was given the Fifth Army Certificate of Achievement.

EXEC OFFICER WRAMC

Colonel Stephen G. Asbill, Veterinary Corps, has been named Executive Officer of the Walter Reed Army Medical Center, Washington. He succeeds Colonel Michael L. Sheppeck who has assumed command of the U. S. Army Hospital, Ft. Leonard Wood, Mo.

Colonel Asbill is the first member of the Veterinary Corps to hold that position. He has been awarded a certificate of proficiency making him a "Logistician, U. S. Army" and as such is the first Veterinary Corps Officer to hold that distinction. Only three

other Army Medical Service officers have attained the coveted Logistician title. Colonel Asbill has spent twenty years of his twenty-six years of military service in the field of logistics.

HONORED

Major General Joseph L. Bernier, Chief of the Army Dental Corps, has been notified of his selection as a Fellow of the famed British Royal Society of Medicine. He is the only American on the list, and the only dental surgeon included with a group of physicians from various parts of the British Empire, as well as Egypt, Teheran, and Ireland. Incidentally he is the only American military dental surgeon ever to have been granted Fellowship in the Royal College of Surgeons of England.

Major Virginia Sage, ANC, USAR, Assistant Director of Nursing Service, D.C. General Hospital, and a member of the 354th General Hospital, U. S. Army, was recently honored when she was chosen as "Nurse of the Year" by the Reserve Officer Association.

First Lieutenant Dorothy M. Berry, ANC, was recently named the honor graduate of the Medical Field Service School's basic military nursing procedures course.

Lt. Berry, a native of North Scituate, R.I., completed her three year nursing training course at Union Memorial Hospital, Baltimore, Maryland, in 1952. Under an Army program she received a B.S. degree from Syracuse University, Syracuse, New York, and then entered on active duty in January 1961. She has been assigned to the William Beaumont General Hospital, El Paso, Texas.

DELIVERS COMMENCEMENT ADDRESS

Major General Elbert DeCoursey delivered the commencement address at the graduation ceremonies of The University of Texas Southwestern Medical School in Dallas on June 8. His address was on "The Scientific Physician-Humanitarian."

General DeCoursey is The Director of the Southwest Foundation for Research and Education, San Antonio, Texas.

RETIRED

Brig. General Henry R. Sydenham, who has been Director of Dental Activities at Brooke Army Medical Center, Fort Sam Houston, Texas, retired from active duty on June 30. The General and Mrs. Sydenham will make their residence in San Antonio at 403 Tomahawk Trail.

Colonel George R. Carpenter, Medical Corps, who has been Chief of the Preventive Medicine Division of the First Army Medical Section, Governors Island, New York, retired recently and has accepted a position with the Health Department of the State of Pennsylvania.

Colonel and Mrs. Carpenter will make their home at 1531 North 2nd Street, Harrisburg.

Lt. Colonel Frank W. Chorpenning, who has been Chief of Immunology and Director of the Blood Bank at Brooke General Hospital, Fort Sam Houston Texas, retired on May 31. He has taken a position on the faculty of the Ohio State University.

Colonel Chorpenning was recently honored by election to membership in the American Association of Immunologists.

POSTGRADUATE DENTISTRY COURSES

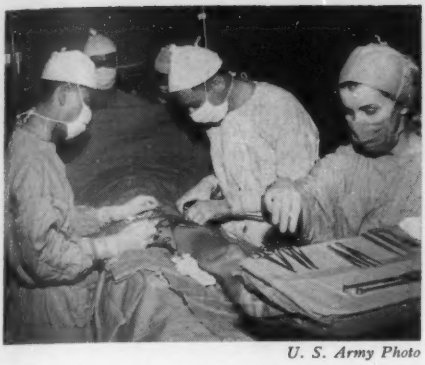
The Army Postgraduate School of Dentistry, Walter Reed Army Medical Center, has announced the following Short Courses: Trends in Dental Laboratory Activities, October 9-11, 1961; Preventive Dentistry, November 6-10, 1961; Prosthodontics, December 4-8, 1961; Oral Surgery, January 8-12, 1962; Oral Diagnosis and Therapeutics, May 14-18, 1962.

Attendance is open to Dental Corps Officers of the Federal Services on active duty and Reserve and National Guard Officers not on active duty.

Applications should be made through regular military channels.

PEOPLE TO PEOPLE PROGRAM

At the 121st Evacuation Hospital in Ascom, Korea, the U. S. Military Assistance Program brings personnel from other lands



U. S. Army Photo

COL. HWANG WAN SON (left), ROK Army surgeon, assists U. S. Army CAPTAIN GEORGE NUGENT in an operation. The surgical nurse is 1ST LT. JEAN SMINDAK. Supervising the anesthetic are 1ST LT. KIM JONG RAE, ROK Army and 1ST LT. AMORIGA, ANC.

to learn our methods and the use of our equipment.

This training takes the form of practical on-the-job experience in all phases of the work of the hospital. Doctors, nurses, surgical technicians and others in the field of medicine come to the 121st for this training which is pursued for a period of from four to six months.

U. S. Army Photo

MAJOR JULIA GAWARECKI (left), USANC, demonstrates an anesthesia machine to 1ST LT. AN JI YOUNG (center) and MAJOR HAM JOHNG UO, ROK Army Nurse Corps.

U. S. Army Photo

(L to R) 1ST. LT. SOPHIA WANG, Republic of China Army Nurse Corps, Corporal KIM CHANG OH, ROK Army, SGT. MALIN KHUNTHAROS of Thailand, and 1ST LT. KIM I, ROK Army Nurse Corps.

Trainees are selected for the program by the governments of their home countries. Salaries are paid by those governments.

There are at present 27 trainees at the 121st from Korea, the Republic of China and Thailand. When these are trained a new group will be sent in, and then another and another. This all spells for good in the People-to-People Program.

Navy

Surgeon General—REAR ADM. EDWARD C. KENNEY

Deputy Surg. Gen.—REAR ADM. ALLAN S. CHRISMAN

TRACHOMA

A vaccine for trachoma has been under study for some time at the U. S. Naval Medical Research Unit in Taipei, Taiwan. Recently, Dr. J. Thomas Grayston reported some of the work on this vaccine at a conference on The Biology of the Trachoma Agent sponsored by The New York Academy of Sciences. Collaborators in the study are Drs. Robert L. Woolridge and San-pin Wang.

An interesting observation was that when

the vaccine was administered after the infection, the severity of the disease was reduced. But when the vaccine was administered prior to infection, it not only failed to protect volunteers against the disease, but appeared to intensify it. Dr. Grayston attributed this to an "allergic type" of reaction. The "allergic" reaction encountered in experimentally infected volunteers did not occur in vaccinated volunteers exposed to natural infection.

RETIRED

Medical Service Corps Officers recently retired were: Lieutenant Commanders Joseph E. M. Daigle and William E. Riley.

PRESIDENT AEROSPACE MED. ASSOC.

Rear Admiral J. L. Holland, MC, USN, Commanding Officer of the Naval Aviation Medical Center, Pensacola, Florida, is the new President of the Aerospace Medical Association. He will serve until April 1962.

Air Force

Surgeon General—MAJ. GEN. OLIVER K. NIESS

Deputy Surg. Gen.—MAJ. GEN. RICHARD L. BOHANNON

FIRST GRADUATION CLASS

Major General Oliver K. Niess, Surgeon General of the U. S. Air Force, delivered the graduation address to the first class that recently completed the new Medical Support for Space Flight at the School of Aerospace Medicine, Brooks Air Force Base, Texas.

This new course is designed to train selected Armed Forces medical officers for future assignments in support of manned space vehicle programs. Students are familiarized with the physical and chemical aspects of the upper atmosphere and space, and the biomedical impact of these factors on man. Also, they learn about present research and development programs concerned with man and his environment during space operations.

General Niess said, "There is an acute need for well-trained flight or space surgeons in the rapidly expanding and demanding field of medical research and development. There is also a growing need for flight surgeons to meet the requirements of the missileers who send the giant missiles aloft. The Mercury, X-15, Minuteman—and soon the Dynasoar program—have already demonstrated to me the requirement for fully trained space-minded flight surgeons. . . .

"We cannot allow all of our energies to be expended in space projects, for we must continue to exert our efforts to saving mankind here on earth. My constant concern is maintaining and improving the health and welfare of our airmen and their families. The enjoyment of the highest standard of health is one of the fundamental rights of every individual without regard to distinction or social position."

STATISTICS

Major General Niess, Surgeon General of the Air Force, recently said that "less than three days a year were lost for duty by our airmen, compared to 1950 when an average of six days was lost by airmen because of illness."

He further reported that in 1960 world wide Air Force medical facilities admitted 398,100 patients and that 67,700 babies were born in Air Force hospitals. More than 12 million outpatients were treated during 1960 in Air Force facilities, and some 215,900 flight physicals were given. Complete physicals, exclusive of flight examinations, reached 429,700, and over seven million immunizations were given.

SCHOOL CHANGES NAME

It is now the School of Aerospace Medicine—the new name for the School of Aviation Medicine.

This institution is 43 years old. It was first known as the Air Service Medical Research Laboratory, Mitchell Field, Long Island, N.Y. Then in 1922 it was named the School of Aviation Medicine.

The School of Aerospace Medicine is headed by Colonel Robert H. Blount and is

located at the Aerospace Medical Center, Brooks Air Force Base, Texas, commanded by Brig. General Theodore C. Bedwell, Jr.

PROMOTED TO BG

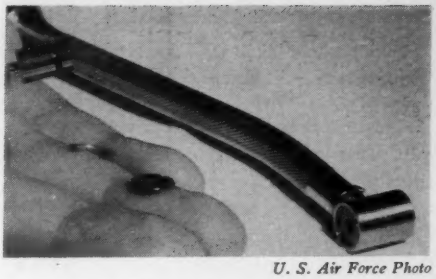
Don S. Wenger, USAF, MC, was recently promoted to the grade of brigadier general. He is assigned as Professional Consultant to the Surgeon General of the Air Force and stationed in Washington.

General Wenger received his academic training at the University of Wisconsin and his medical degree from Marquette University. He holds an M.S. degree granted him by Georgetown University. He is a Senior Flight Surgeon, Fellow of the American College of Surgeons, and the International College of Surgeons.

HIGH SPEED DENTAL HANDPIECE

A 260,000 rpm air bearing, air turbine dental handpiece was recently delivered to the School of Aerospace Medicine, Brooks Air Force Base, Texas, for use in the dental research branch.

Extremely low vibration and noise levels are features of the new handpiece. These are factors contributing to greatly lessened discomfort for dental patients, and fatigue for the dentist. The higher speeds require almost no pressure and reduce tooth contact time by 75 percent. In spite of this high speed attained it is only a milestone toward much higher speeds which are sought by the Air Force dental research personnel at the School.



U. S. Air Force Photo

The high speed dental handpiece.

U. S. Air Force Photo

(L to R) Lt. Col. Jack J. Hartley, USAF, DC, technical director; and Col. Carlos F. Schuessler, USAF, DC, Chief, Dep't., Dental Sciences, Aerospace Medical School, inspect dental handpiece delivered by Gene L. Green and Richard E. Born, Garrett Corp.

TOWARD BETTER FOOD

A two-day conference to improve the training methods for food service personnel in Air Force hospitals was recently held in the Office of the Surgeon General. Miss Grace Stumpf, University of Michigan, the National Dietetic Consultant to the Surgeon General, assisted personnel of his office in conducting the program.

USAF Photo

Seated (L to R) Miss Grace Stumpf; Col. A. A. Underkofler, USAF, MSpC, Chief of the Medical Specialist Corps; Standing (L to R) Capt. Ernestine Neuhardt, USAF, MSpC, Wright-Patterson AFB, Ohio; Capt. Jean T. McKay, USAF, MSpC, Office of Surgeon General, USAF.

CONTOURATOR

The development of the modified Dental Contourator at the School of Aerospace

Medicine in the Aerospace Medical Center at Brooks Air Force Base, Texas, will open the way to better oral surgery, prosthodontic and periodontal studies.

A contourator is an instrument that permits accurate measurement of dental casts showing tissue changes. Those desiring a technical report and blueprints on the contourator may obtain same by writing the School, attention RSCH.

Public Health Service

Surgeon General—LUTHER L. TERRY, M.D.

Deputy Surg. Gen.—JOHN D. PORTERFIELD, M.D.

NEW DENTAL BUILDING—NIH

A new building for the laboratories of the National Institute of Dental Research was dedicated May 26 at Institutes Center, Bethesda, Maryland. Dr. Francis A. Arnold, Jr., Director of the Dental Institute, presided. Dr. Emory W. Morris, President of the W. K. Kellogg Foundation of Battle Creek, gave the principal address.

This $4 million building was designed to house the scientific and administrative operations of the National Institute of Dental Research.

NURSE RESEARCH FELLOWSHIPS

Nurses with baccalaureate degrees and an interest in research may be eligible for fellowships in the Nurse Research Fellowship program of the Public Health Service.

Since 1955, 117 nurses have received full-time fellowships and over 100 have had part-time awards; the Public Health Service expenditure for this purpose has exceeded $750,000.

Nurses who wish to apply for special predoctoral fellowships may obtain application forms from the Division of Nursing, U. S. Public Health Service, Washington 25, D.C.

CONFERENCE—MEASLES IMMUNIZATION

An international conference on measles immunization will be held November 7 through 9 at the National Institutes of Health, Bethesda.

The conference is under the joint sponsorship of the University of Colorado, the National Institute of Allergy and Infectious Diseases, and the Division of Biologics Standards. Plans are under the direction of Dr. C. Henry Kempe, Professor and Head of the Department of Pediatrics, University of Colorado Medical Center.

Measles is a world-wide problem. Almost 100% of the children in the United States can be expected to contract this disease and there are several hundred deaths a year attributed to measles. The mortality in some countries reaches ten percent or more. Consequently there is a great interest in immunizing against the disease.

PRIMATE RESEARCH CENTERS

The University of Wisconsin and the University of Washington have been given grants totaling $3,203,554 for the construction and operation of Primate Research Centers.

Surgeon General Luther L. Terry said, "All sciences concerned with mental and physical disorders in man may someday benefit from the existence of facilities such as these."

AIR POLLUTION

Lead levels—in the air and in the human system—will be studied by health and air pollution authorities in Philadelphia, Los Angeles, and Cincinnati. These studies are the outgrowth of recommendations on tetraethyl lead made by a special advisory committee to the Surgeon General of the Public Health Service.

VD

Early infectious syphilis reported in the United States has risen 87% since 1958 according to reports. To put it in numbers it is a rise from 6,661 cases to 12,471 cases. For the quarter July-September 1960 there were 4,508 cases, representing a 72.2% increase.

Remember the days when the word

"syphilis" could not be mentioned on the radio? Now that the disease can be mentioned it might be one way to bring the dangers of the disease and its increase in prevalence again to the ears of the American people. And while that is being done why not mention the other venereal diseases?

PUBLICATION

Cataract and Glaucoma (PHS Publ. No. 793) explains to the public some of the facts about these diseases. This is a good brochure for the doctor's office. Price 15¢ each. Obtained from the Government Printing Office, Washington.

The Costly Time Lag (PHS Publ. No. 813) is an informative booklet designed to encourage wider use of the health-saving knowledge that has resulted from the findings of medical research. Copies can be obtained from the Government Printing Office, Washington, for 20¢ a copy.

Reporting of Hospitalization (PHS Publ. No. 584-D4) is a recent release from the U. S. National Health Survey. This is a 71-page book which can be obtained from the Government Printing Office for 50¢ a copy.

The Dog in Medical Research, a brochure now in its third edition, is available free from the Public Health Service, Washington. Bulk orders of this publication (PHS Publ. No. 312) can be obtained from the Superintendent of Documents, Government Printing Office, Washington 25, D.C., at 15¢ per copy.

Contents include sections on sources of animals; selection for special purposes; care and handling; quarters; feeding, and humane treatment. A list of guiding principles is featured, as well as a model pound law for local jurisdictions. New features are the section on humane treatment and a list of organizations interested in the care of laboratory animals.

Veterans Administration

Chief Medical Director—WILLIAM S. MIDDLETON, M.D.

Deputy Chief Med. Dir.—H. MARTIN ENGLE, M.D.

APPOINTMENT

Dr. H. Elston Hooper has been appointed chief of psychology research for the Veterans Administration, Washington, D.C. He will coordinate the agency's research in psychology nationwide.

The program includes more than 800 studies. It is one of the nation's major research attacks on mental illness and the psychological components of physical disease.

Dr. Hooper served in the military forces from 1942 to 1946. He served as clinical associate professor of psychology at the University of Southern California and director of the Psychological Service Center at Redondo Beach, California. Recently he has been chief of the central research laboratory at the Augusta, Georgia, Veterans Administration Hospital.

ASSIGNMENT

Dr. George R. Clammer, who has been director of professional services at the VA hospital, Philadelphia, has been appointed manager of the Veterans Administration Hospital at Fort Wayne, Indiana. He served in the Army Medical Corps from November 1950 to November 1952.

Dr. Robert J. Scott, who has been manager of the Fort Wayne VA hospital has been transferred to the Richmond (Va.) Veterans Administration hospital as its manager.

ELECTED CHAIRMAN

Dr. Austin W. Berkeley, professor of psychology and chairman of the Department of Psychology, Boston University Graduate School, has been elected Chairman of the Veterans Administration Area Psychology Advisory Council.

The Council which is affiliated with the Veterans Administration is approved by the American Psychology Association for graduate level Doctor of Philosophy training in Psychology.

Besides Boston University, other universities represented on the Area Council are: Adelphi (College), Buffalo, Clark, Columbia, Connecticut, Harvard, Massachusetts, New York, Rochester, Syracuse and Yale.

DEFENSE AND DISASTER RELIEF PLANNING

The Veterans Administration estimated that in a national emergency its 170 hospitals and 91 out-patient clinics could provide care and medical facilities for 350,000 patients. As would be true for any medical installation "only the most austere care could be provided" during such emergencies.

TESTING FOR TB

Tests from 96 patients of the Minneapolis VA hospital show that a new method is more accurate than examining stomach washings for the presence of the tubercle bacillus. The method is also more pleasant. Material can be tested the same day whereas stomach washings are usually cultured and a number of days are required before the cultures can be examined.

By having a patient inhale a warm mist of ordinary table salt and glycerin, sputum can usually be obtained readily.

The method was reported to the Research Conference in Pulmonary Diseases held recently by the Veterans Administration and the Armed Forces by Dr. James P. Lillehei of the University of Minnesota School of Medicine and the Minneapolis VA hospital.

Miscellaneous

ELECTED PRESIDENT

Dr. Edmund G. Beacham, Chief of the Tuberculosis Division, Baltimore City Hospitals, was elected President of the Maryland Tuberculosis Association at a recent meeting. He has been a member of the Board of Directors of the Association since 1954.

A graduate of the University of Maryland School of Medicine, Dr. Beacham is a Fellow of the American College of Physicians, a Fellow of the American College of Chest Physicians, and a member of the Executive Council of the Association of Military Surgeons.

PAHO HEADQUARTERS BUILDING

The Pan American Health Organization (PAHO) has been offered $3.75 million by the W. K. Kellogg Foundation of Battle Creek, Michigan, for the construction of a permanent headquarters building at 23rd Street and Virginia Avenue, N.W., Washington. This is close to the George Washington University and the proposed National Cultural Center.

The offer has been made with the provision that PAHO's Member Governments appropriate an equal amount to expand and accelerate the Organization's health program in the Americas.

Construction of the building is expected to begin in 1962 and will involve the expenditure of about $4.5 million.

SIX YEARS FROM HS TO MD

Boston University will inaugurate a new unified six-year program leading to the doctor of medicine degree, effective this fall.

The plan was originally instigated by a $50,000 grant from the Rockefeller Foundation to the Boston University School of Medicine in 1956. A $600,000 grant from the Commonwealth Fund of New York to help underwrite the costs of the first four years will make it possible to launch the program this fall.

So interested in this is the National University of Iran that they have asked Dr. John J. Byrne, professor of surgery at Boston University School of Medicine to visit that country this summer to help formulate the curriculum for its new medical school.

Dr. Byrne is on the board of editors of the *New England Journal of Medicine.*

INTRAVENOUS TECHNIQUE LEGAL

Registered nurses in the State of New York are now authorized under doctor's supervision to give blood transfusions, intravenous injections, infusions and other "I.V." procedures. By this ruling of Attorney General Lefkowitz, New York State has taken the leadership in clarifying the State Nurse Practice Act to include intravenous technique as a professional nursing function. See Squibb *Nurses Notes,* Vol. 10, No. 2, March-April, 1961.

DRUGS FROM OVERSEAS

"The Military Medical Supply Agency and

the Veterans Administration have sent millions of the taxpayers' dollars overseas to purchase cheap, pirated versions of powerful drugs discovered by U.S. companies and presumably protected by U.S. patents. This practice was deservedly denounced by American labor when the Oil, Chemical, Atomic Workers International Union passed a resolution strongly condemning it. When the government goes shopping, the taxpayer has a right to expect that it will spend his money wisely, for a good purpose and for the general welfare of the country." Words of U.S. Senator Hugh Scott in 87th Congress. As printed in *Medicine at Work,* Vol. 1, No. 6.

Incidentally the Military Medical Supply Agency is *not* headed by a medical person or one of the allied branches of medicine. The Navy Supply Corps provides personnel for the key positions.

SPACE MAN

The Chemacon Backpack is an individual air-conditioner for the space man. It uses a battery-powered blower to circulate air through a pressure suit. Heat, moisture, carbon dioxide and odors are removed. Oxygen is added in the correct proportion and the air is returned to the pressurized suit. Such a device will provide free movement of the space man in any space vehicle.

MSA Research Corp

CHEMACON BACKPACK

CLEFT PALATES

Cleft palate patients with no teeth now will be able to satisfactorily correct their speech defects through a unique magnetic device created in the Cleft Lip and Palate Institute of Northwestern University, Chicago. The apparatus was recently described by Dr. Morton S. Rosen, assistant professor of prosthetic dentistry.

He emphasized that the apparatus is effective only for patients with fairly wide cleft.

DISEASES OF LABORATORY ANIMALS

A symposium, the first of a planned series on the diseases of laboratory animals, will be held in Detroit, Michigan, August 24, in conjunction with the annual convention of the American Veterinary Medical Association. Arrangements have been made by the American Board of Laboratory Animal Medicine, Argonne, Illinois.

PULMONARY DISEASE SYMPOSIUM

Fitzsimons General Hospital, Denver, Colorado, will be the host to the Fourteenth Annual Symposium on Pulmonary Disease to be held September 25-29.

This Symposium is co-sponsored by the American Thoracic Society, the University of Colorado School of Medicine, and Fitzsimons General Hospital. Registration fee is $5.00.

Further information may be obtained from the University of Colorado Medical School, Denver, or from the Program Director, Colonel Charles S. Christianson, Pulmonary Disease Service, Fitzsimons General Hospital.

ANIMAL CARE PANEL

The 12th Annual Animal Care Panel Meeting will be held in Boston, September 27, 28, and 29 at the Statler Hilton Hotel. Bernard F. Trum, D.V.M., Harvard Medical School, is the general chairman.

PROJECT HOPE

A film, "Voyage of the SS HOPE," tells the story of this floating medical center in Indonesia waters. The film is a 27-minute color motion picture with narration by Bob Considine.

Prime mover of Project Hope is Dr. William B. Walsh of Washington, D.C., who points out that the project is one of the American people and is supported by them through contributions.

The film can be obtained from Project HOPE, 1818 M St., N.W., Washington 6, D.C.

RADIOACTIVITY MEASURING INSTRUMENT CATALOG

A new 96-page catalog (S), describing more than 250 instruments, is available to educators, physicians, biochemists, and industrial researchers on request to Nuclear-Chicago Corporation, 359 East Howard Ave., Des Plaines, Ill.

MERCK MANUAL

The tenth edition of *The Merck Manual* is off the press. The new book contains 1900 pages. Regular edition is $7.50; deluxe edition—$9.75. Order from Merck & Co., Inc., Publications Dept., Rahway, N.J.

SYLLABUS AVAILABLE

Syllabus of Dermal Pathology, Inflammatory Dermatosis, Course #1, by H. Montgomery, M.D. and E. B. Helwig, M.D., has been reprinted and is now available from the American Registry of Pathology, Armed Forces Institute of Pathology, Washington 25, D.C. Price is $2.00.

INFLUENZA

An annotated *Bibliography of Influenza* is available for $2.00 a copy from the American Institute of Biological Sciences, 2000 P St., N.W., Washington 6, D.C.

ALL AMERICAN

Where Washington gives Washington takes.

Honor Roll

Colonel Frank K. Lawford, MSC, USA
Dr. Kenneth Classen (Capt.)
Capt. Edgar R. Palarea, MC, USAF
Lt. Col. Wm. R. Bunge, MC, USA
Lt. Col. Edward A. Barrett, MC, USAR
1/Lt. Evelyn Bedard, NC, USAF
Israel Hanenson, M.D.
Col. Louis N. Altshuler, MC, USA
Capt. C. P. Phoebus, MC, USN
Lt. Col. Leonard D. McLin, MC, USAF
Colonel Louis E. Mudgett, MSC, USA

New Members

Capt. Joanne Seymour, NC, USAF
Capt. Robert E. Walsh, MC, USN
LCdr. A. W. Ondreasen, USPHS (R) (Inact.)
1/Lt. John W. O'Brien, ANC, USAR
Maj. Mary E. Steinheimer, MC, USA
Maj. Jeanne M. Treacy, ANC, USA
Capt. A. Herbert Schwartz, MC, USAF
Major George M. Stewart, MC, USAR
Lt. Matthew K. Becker, MC, USN
Med. Dir. Robert E. DeLashmutt, USPHS
Capt. William K. Pyle, MSC, USA
Capt. Herbert Alexander Dillard, MSC, USAR
V. A. Pharm. Vera T. Wittenberg
Captain Francis L. Comunale, MC, USA
Major Nickolas F. Kobylk, MSC, USAF
Captain Vance E. Senter, MC, USN
Captain Kenneth E. Gough, MSC, USA
Capt. John H. Young, Jr., MSC, USA
1st Lt. Richard C. Dickson, MSC, USA
Major Philip R. Casesa, MC, USAR
Lt. Col. William M. Chardack, MC, USAR
Col. John Staige Davis, Jr., MC, USAR
Captain Philip J. McNamara, MC, USN
Lt. Col. Myron Frank Sesit, MC, USAR
Captain Joseph J. Timmes, MC, USN
Col. Herman L. Weisler, DC, USAR
Lt. Col. Morris V. Olson, MSC, USA
1/Lt. Robert Visser, MSC, USA
Cdr. Aldo Edward Gillotte, DC, USNR

Maj. Herbert A. Logan, MSC, USA
Sr. Surg. Charles M. Grace, USPHS
Maj. James S. Knorr, MSC, AUS, Ret.
Capt. Kathleen J. Mahoney, NC, USAF
Lt. Col. Robert O. Stone, MSC, USA
Capt. Bruce E. Green, MSC, USA
Maj. Billy C. Greene, MSC, USA
1/Lt. Turman E. Allen, Jr., MSC, USA
Maj. John J. Graff, MC, USA
Lt. Beverly J. Slater, NC, USN
1/Lt. Joseph Dubiel, Jr., MSC, USA
Capt. Aaron Weisberg, MC, USA
Lt. Col. James A. Bornman, MSC, USAR
Capt. Norman H. Moore, MC, USAF
Lt. Col. Thomas E. Baker, MSC, USA
Maj. Elio Sanchez, MC, Cuban Army, Ret.
Capt. Sarah B. Twitty, ANC
Capt. Donald E. Wallis, MC, Tenn. Air NG
Major Alfons C. Groth, MSC, USA

MEMBERSHIP COMMITTEE

Commander Calvin F. Johnson, MSC, U. S. Navy, Chairman
Mr. George F. Archambault, U.S.P.H.S.
Commander Burdette M. Blaska, NC, U.S.N.
Colonel Jesse W. Brumfield, MSC, U. S. Army
Lt. Col. Nathan Cooper, U. S. Air Force (MSC)
Lt. Col. V. Harry Adrounie, USAF, MSC
Mr. Vernon O. Trygstad, Veterans Administration

Deaths

LAUDERDALE, Clarence E., Major, Dental Corps, U. S. Army, Retired, died at the age of 87, at Pasadena, California.

Doctor Lauderdale was one of the first 30 contract dental surgeons employed by the Army at the turn of the century, and was among the first dental officers to be commissioned in the Dental Corps when it was formed 50 years ago.

He is survived by his wife, two sons, and two daughters. One of his sons, Major James M. Lauderdale, is an Army Medical Corps officer on duty at Fort Huachuca, Arizona.

ORR, Louis M., Colonel, Medical Corps, AUS, during World War II, and immediate past President of the American Medical Association, died May 23 at his home in Orlando, Florida. His age was 61.

Doctor Orr was a noted urologist. He had served in the armed forces in World War I. He received his medical degree from Emory University in 1924. In 1946 he received the Sullivan Award from Rollins College, Winter Park, Florida.

PRATHER, Victor A., Jr., Lieutenant Commander, Medical Corps, U. S. Navy, was killed May 4, 1961, while being rescued from the Gulf of Mexico by a helicopter after he had participated in a record 21.5 mile balloon ascent. His age was 34.

Doctor Prather received his medical degree from Tufts University School of Medicine (1952).

He is survived by his widow, 8008 Beech Tree Road, Bethesda, Maryland.

SMITH, Orne D., Lt. Colonel, MSC, U. S. Army, died April 30 at his home in Arlington, Virginia, after a heart attack. His age was 47.

Colonel Smith, a native of St. Paul, Minn., was on duty in the Office of the Surgeon General of the Army as Chief of the Career Planning Branch of the Personnel and Training Directorate. He entered the military service in 1942 and had served in Italy, Japan and Korea.

He is survived by his widow, 4900 Old Dominion Drive, Arlington, and three daughters.

STYLES, Jean Eleanor, Captain, Army Medical Specialist Corps, died April 12 while on leave at her home in Wayne, New Jersey. Age 35; death was due to cancer.

Captain Styles was commissioned in the Army Medical Specialist Corps in 1948. She had been stationed at Valley Forge General Hospital, Phoenixville, Pa., as an occupational therapist since October 1957.

She is survived by her parents, Mr. and Mrs. S. O. Styles, 40 Styles Terrace, Wayne, N.J., and a sister, Mrs. Donald Walls of Washington, D.C. Interment was at Pine View Cemetery, Glens Falls, N.Y.

NEW BOOKS

Blood Platelets. Henry Ford Hospital International Symposium. Editors: Shirley A. Johnson, Ph.D., Raymond W. Monto, M.D., John W. Rebuck, M.D., Ph.D., and Robert C. Horn, Jr., M.D. Little, Brown and Company, Boston. Price $18.50.

Disease and Injury. Edited by Leopold Brahdy, M.D. J. B. Lippincott Company, Philadelphia, Montreal. Price $12.50.

Symptom Diagnosis. 5th Ed. By Wallace Mason Yater, A.B., M.D., M.S. (in Med.), F.A.C.P., and William Francis Oliver, B.S., M.D., F.A.C.P. Appleton-Century-Crofts, Inc., New York. Price $15.00.

Somatic Treatments in Psychiatry. By Lothar B. Kalinowsky, M.D., and Paul H. Hoch, M.D. In collaboration with Brenda Grant, M.D., D.P.M. Grune & Stratton, New York, London. Price $9.75.

Health Organizations of the United States and Canada: National, Regional and State. A Directory of Voluntary Associations, Professional Societies and Other Groups Concerned with Health and Related Fields. By Clara Sedacca Wasserman with Paul Wasserman. Graduate School of Business and Public Administration, Cornell University, Ithaca, N.Y. Price $10.00.

The Management of the Doctor-Patient Relationship. By Richard H. Blum, Ph.D. With Foreword by Joseph Sadusk, M.D. and Rollen Waterson. 304 pp. McGraw-Hill Book Co., New York. Price $8.50.

The Heinz Handbook of Nutrition. By Benjamin T. Burton, Ph.D., Executive Editor. 447 pp., illustrated. McGraw-Hill Book Co., New York. Price $5.75.

Science and Psychoanalysis. Vol. IV: Psychoanalysis and Social Process. Edited by Jules H. Masserman, M.D.; 29 contributors. 196 pp. Grune & Stratton, New York, London. Price $6.75.

Essentials of Neurology. By John N. Walton, M.D., M.R.C.P. 422 pp. J. B. Lippincott Co., Philadelphia, Montreal. Price $6.75.

Cell and Tissue Culture. 2nd Ed. By John Paul, M.B., Ch.B., Ph.D., M.R.C.P. Ed. 312 pp., illustrated. The Williams & Wilkins Co., Baltimore. Price $7.50.

Progress In Clinical Surgery. Series II. Edited by Rodney Smith, MS., F.R.C.S.; 23 contributors. 327 pp., 110 illustrations. Little, Brown and Company, Boston. Price $11.50.

Essential Pathology. By Roger D. Baker, M.D. 638 pp., illustrated. The Williams & Wilkins Co., Baltimore. Price $9.50.

Psychology as Applied to Nursing. 2nd Ed. By Andrew McGhie, M.A., Ph.D. With Foreword by Margaret C. N. Lamb, R.G.N., S.C.M. 266 pp. The Williams & Wilkins Co., Baltimore. Price $4.50.

Systematic Observation of Gross Human Behavior. By G. R. Pascal and W. O. Jenkins, 126 pp. Grune & Stratton, New York, London. Price $4.75.

The Treatment of Tropical Diseases. By W. H. Jopling, M.R.C.P. (Lond.), M.R.C.P. (Edin.), D.T.M. & H. (Eng.). 202 pp. The Williams & Wilkins Co., Baltimore, exclusive U. S. agents. Price $5.00.

Recognizing the Depressed Patient. With Essentials of Management and Treatment. By Frank J. Ayd, Jr., M.D. 138 pp. Grune & Stratton, Inc., New York, London. Price $3.75.

Style Manual for Biological Journals. Prepared by the Committee on Form and Style of the Conference of Biological Editors. 92 pp. American Institute of Biological Sciences, Washington, D.C. Price not stated.

Orthopaedic Approaches: A Stereographic Manual. Section I: Lower Extremity. With Reels 1 to 18. By John J. Joyce, III, M.D., B.A., and Michael Harty, M.A., M.B., M.Ch., F.R.C.S. (Eng.). 80 pp., illustrated. The Williams & Wilkins Co., Baltimore. Price $28.00.

Clinical Methods of Neuro-Ophthalmologic Examination. 2nd Ed., completely revised and enlarged. By Alfred Kestenbaum, M.D. 577 pp., illustrated. Grune & Stratton, Inc., New York, London. Price $16.75.